JOURNAL

of the

INDIAN MEDICAL ASSOCIATION

VOLUME 45 NUMBER 7 CALCUTTA OCTOBER 1, 1965

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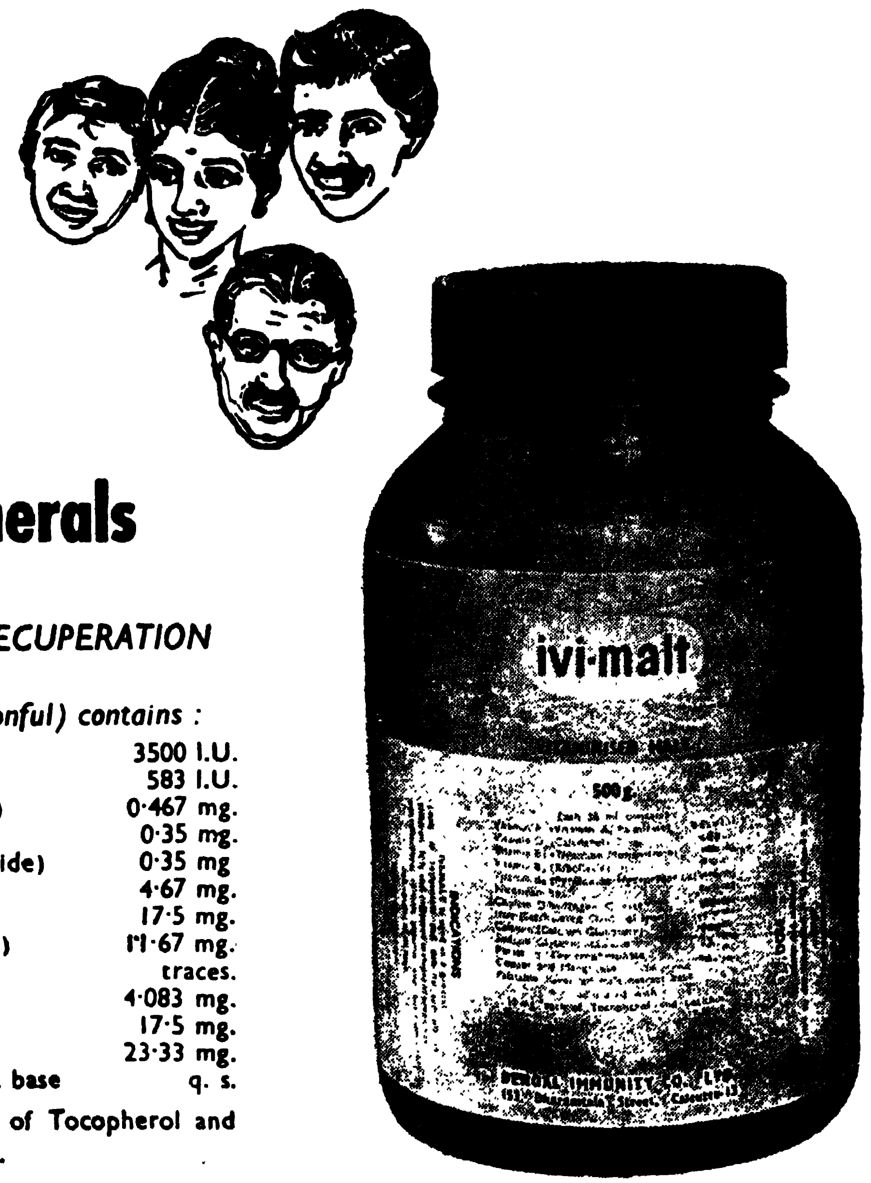

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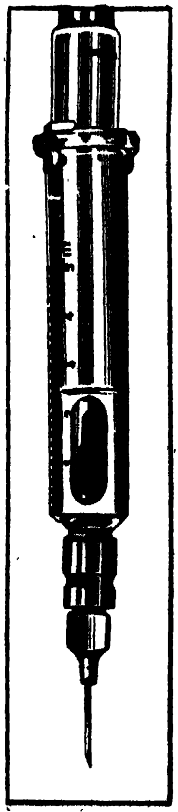

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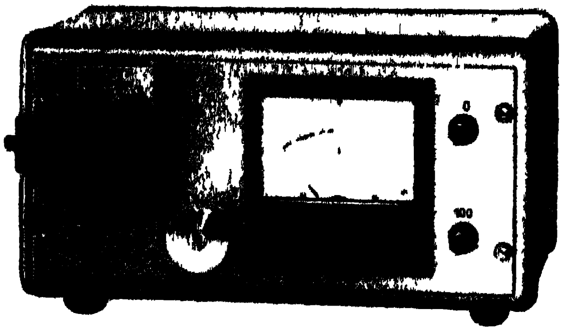

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[1] A. Bryan Wade, B Ch D., F D S., G C Blake, M B., B S., F D S., J D Manson, M.Ch D., F.D S., John K. Berdon, B S., D D S., M D S., Freda Mathieson, B Ch D Diana M. Bate, B.D. S Treatment of the Acute Phase of Ulcerative Gingivitis (Vincent's Type) a comparative Assessment of the Use of Sodium Peroxyborate Monohydrate and Penicillin. British Dental Journal Vol. 115, No. 9 pp 372-375 November 5, 1963.

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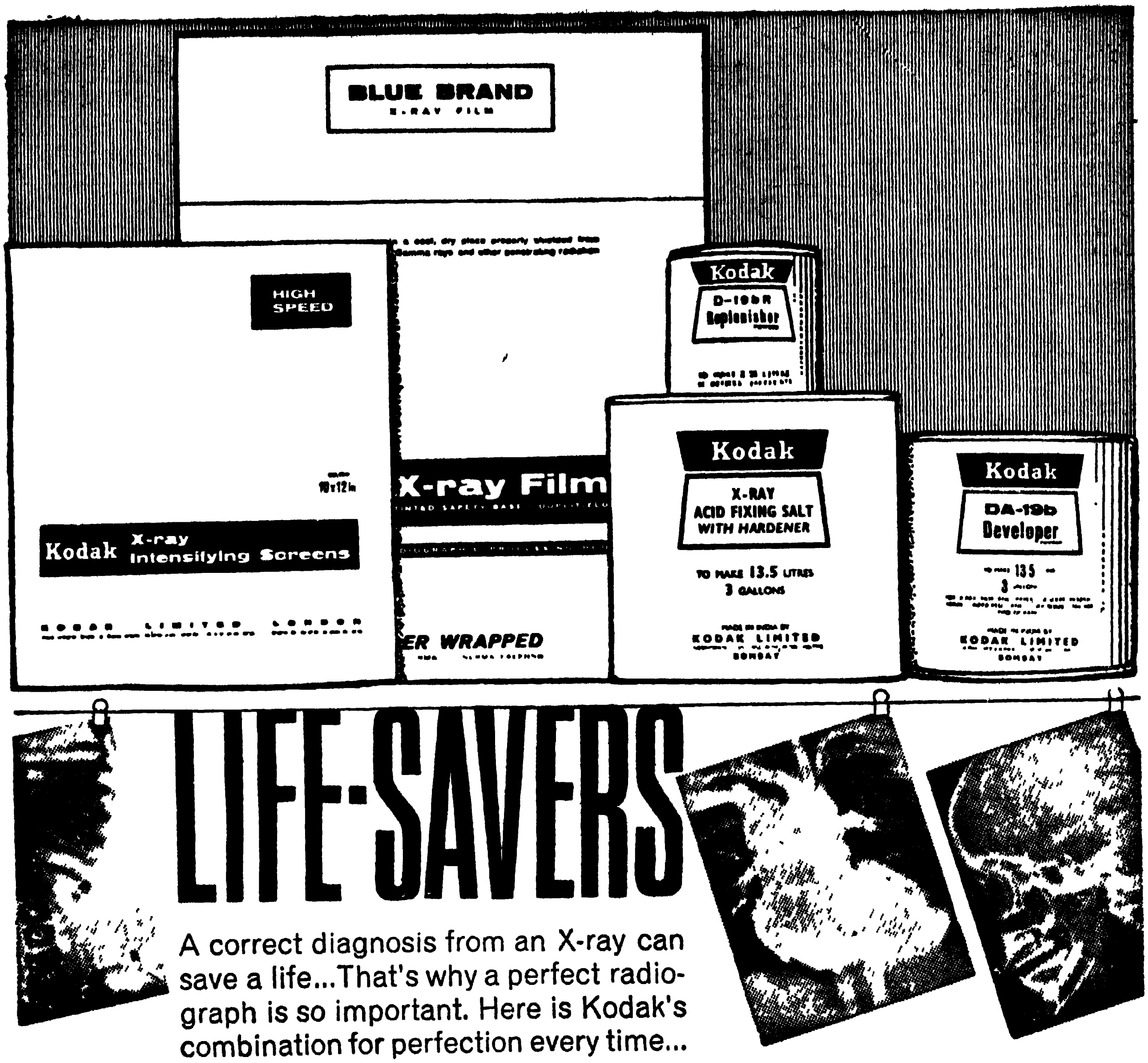

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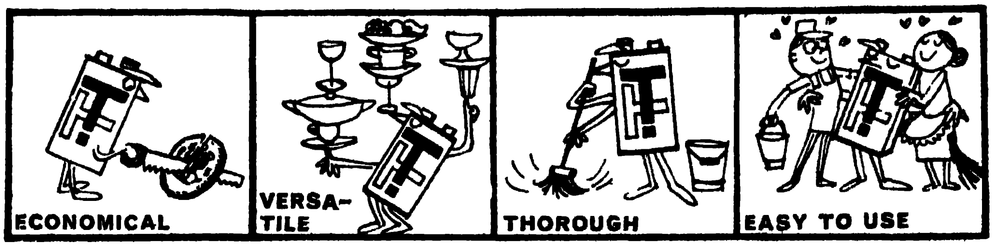

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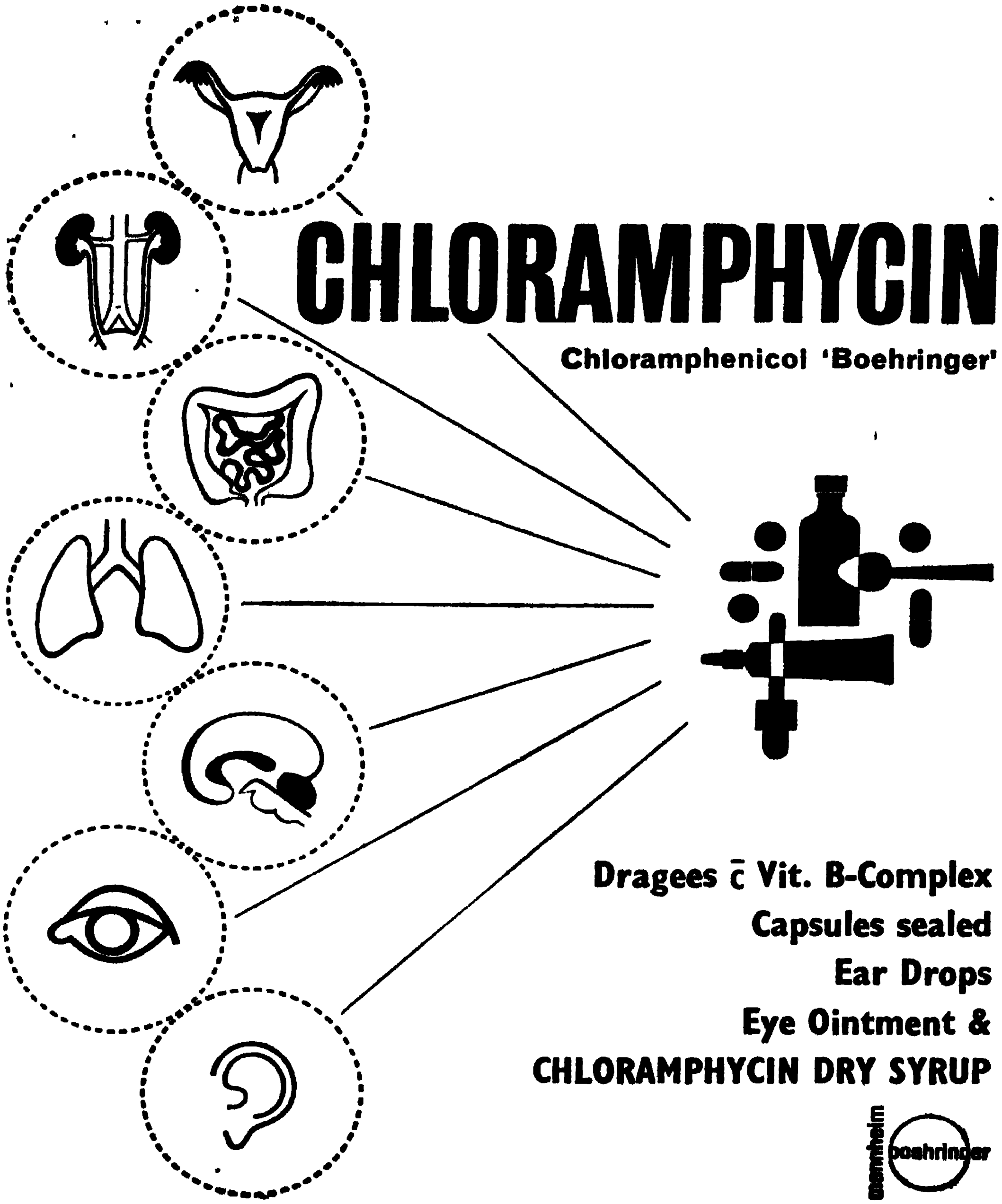

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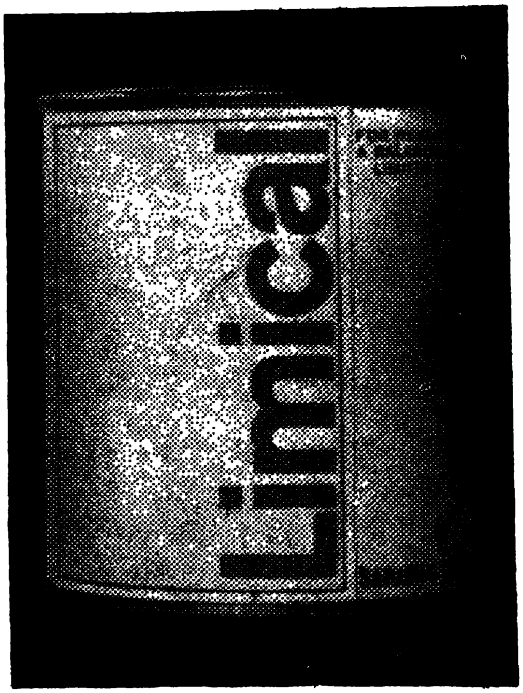

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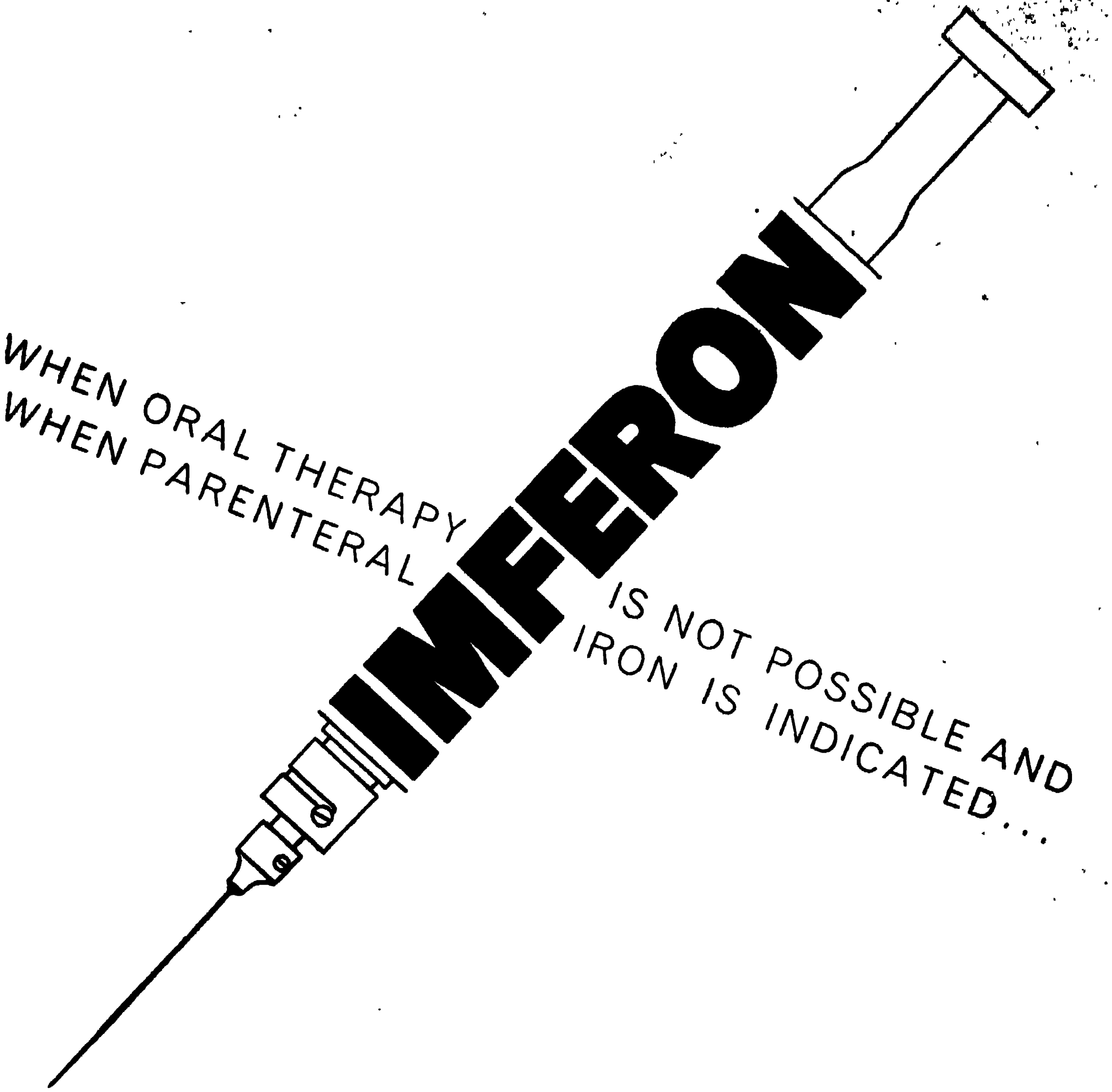

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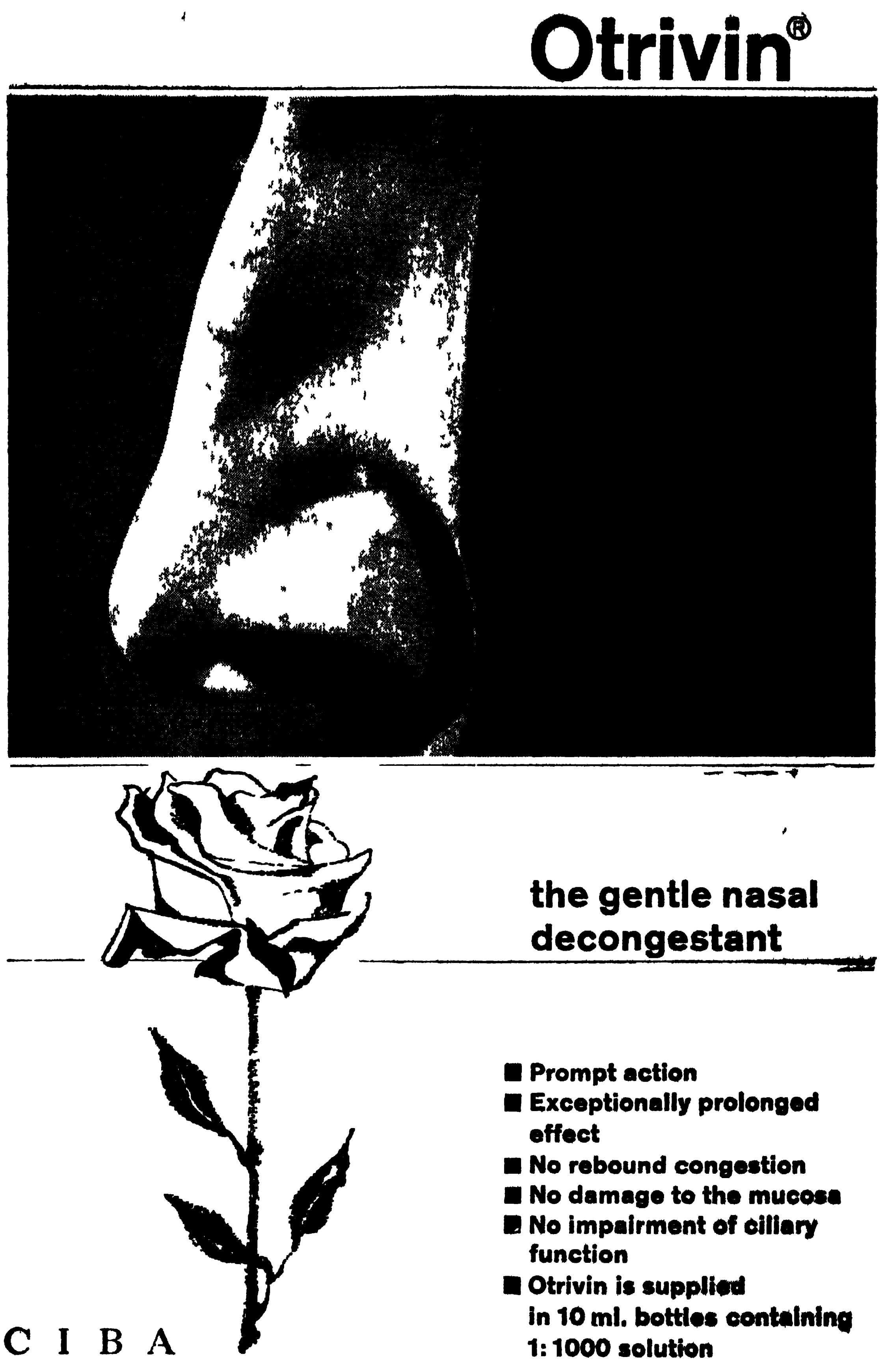

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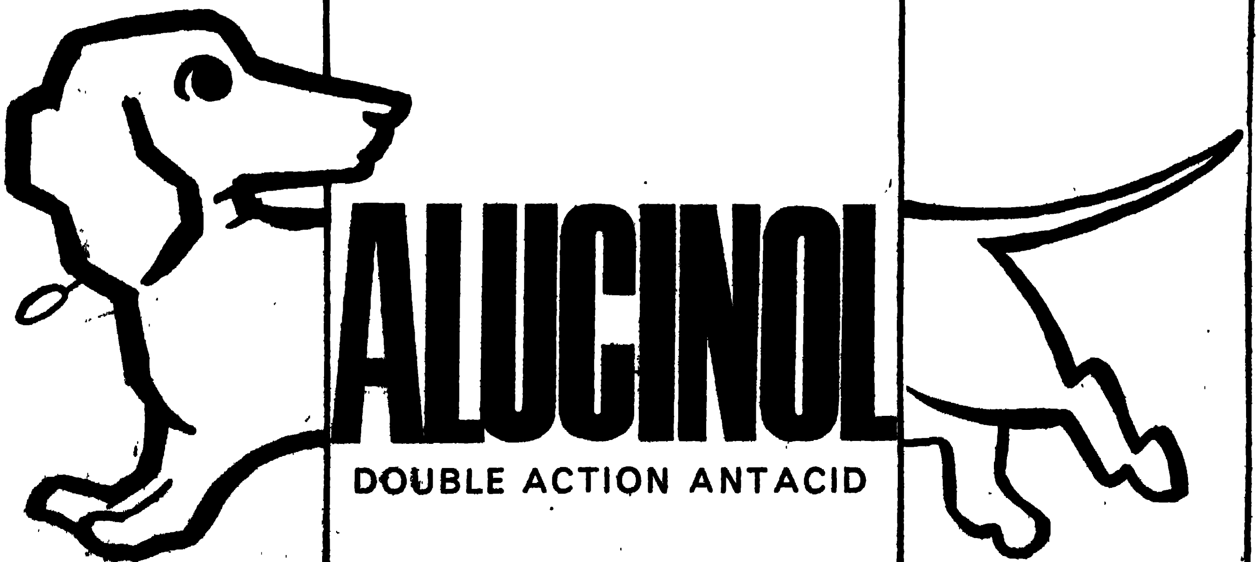

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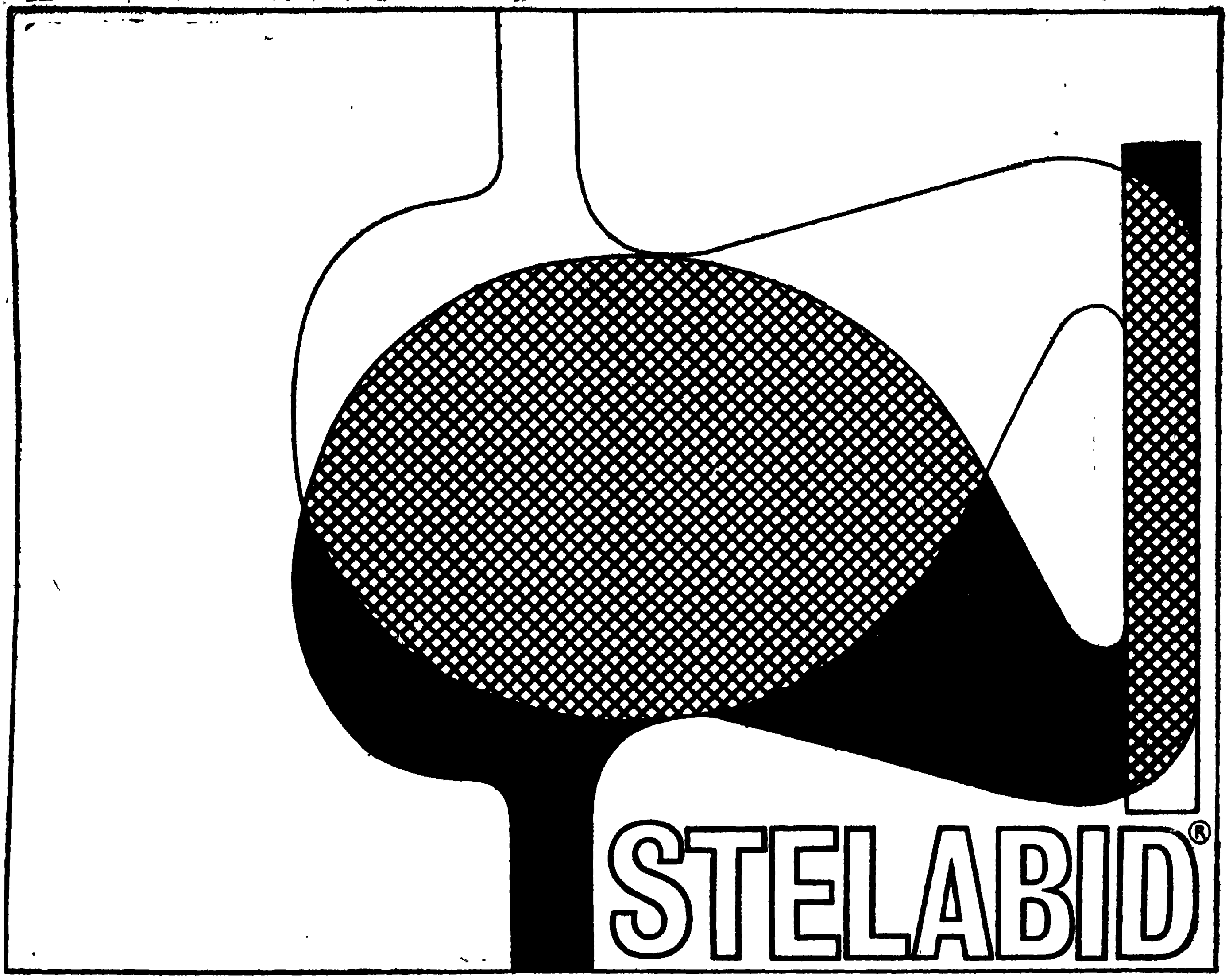

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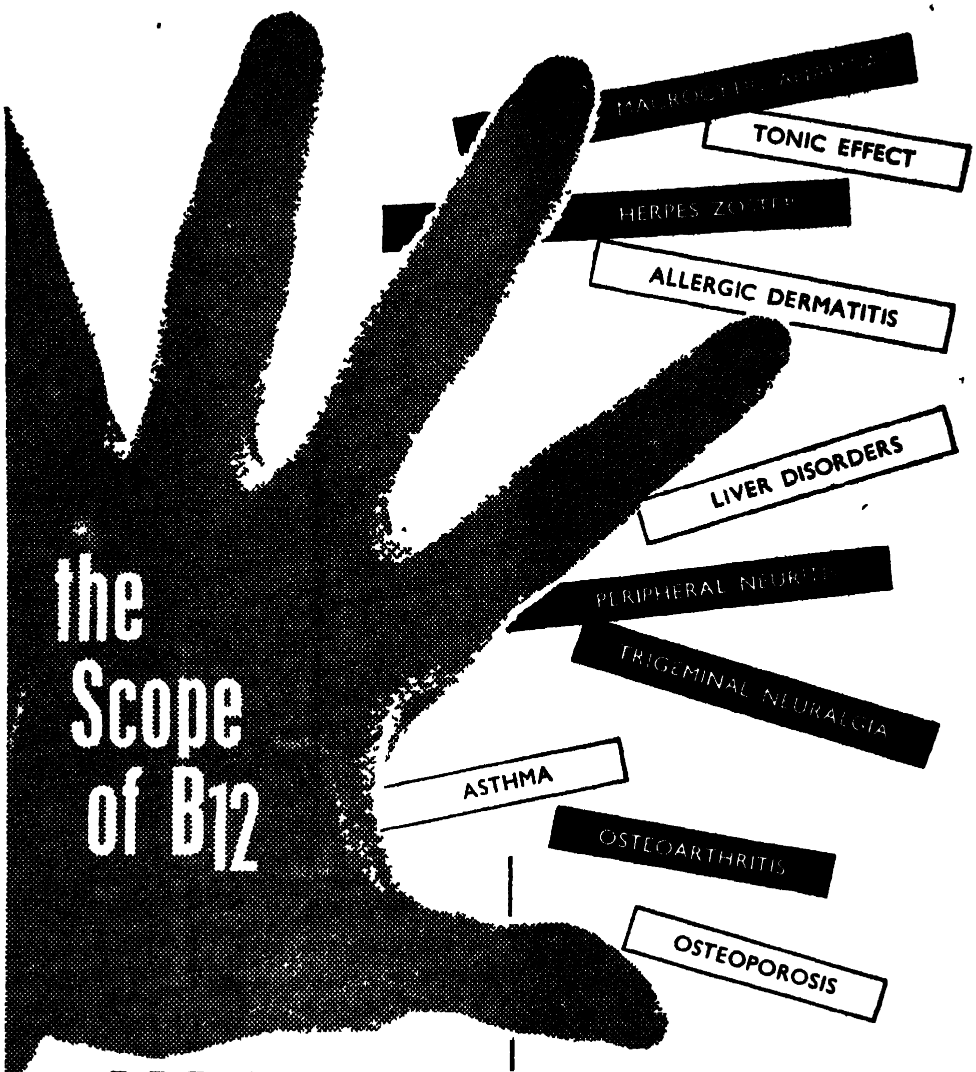

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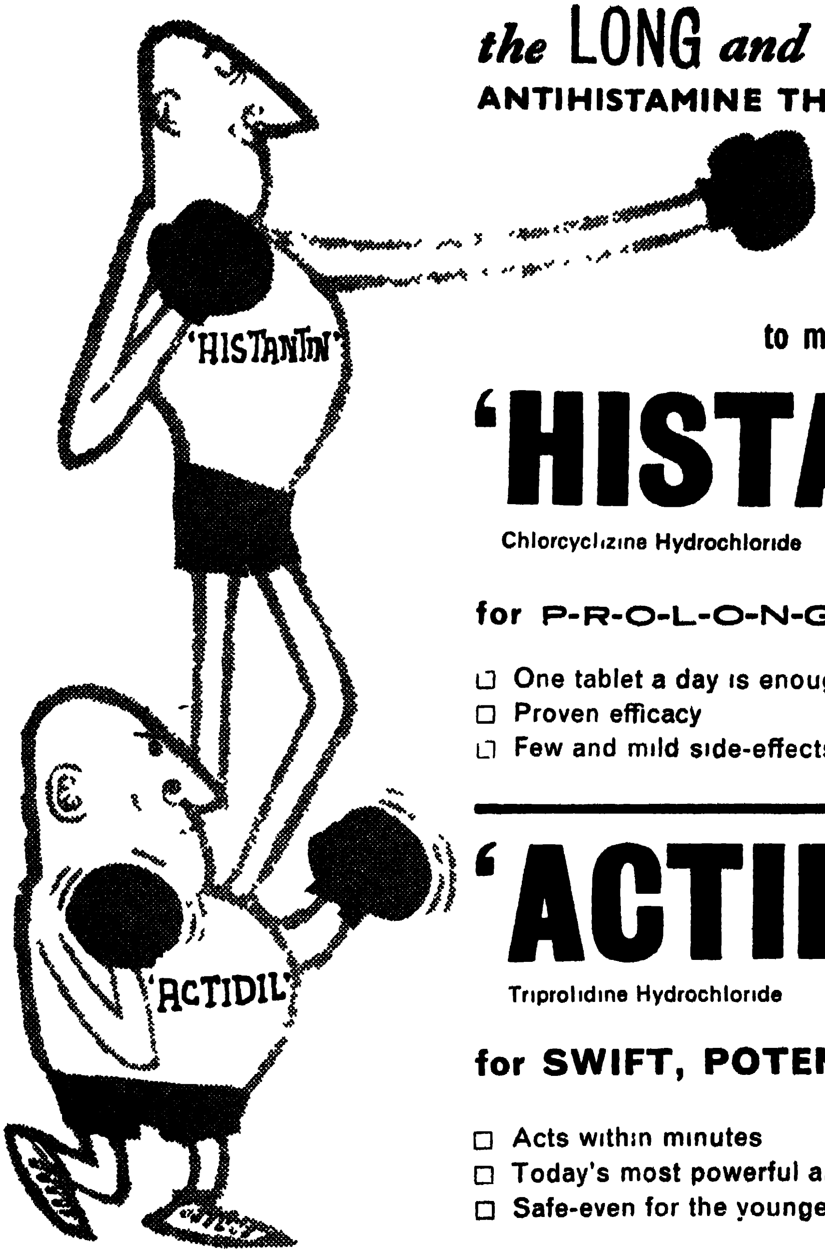

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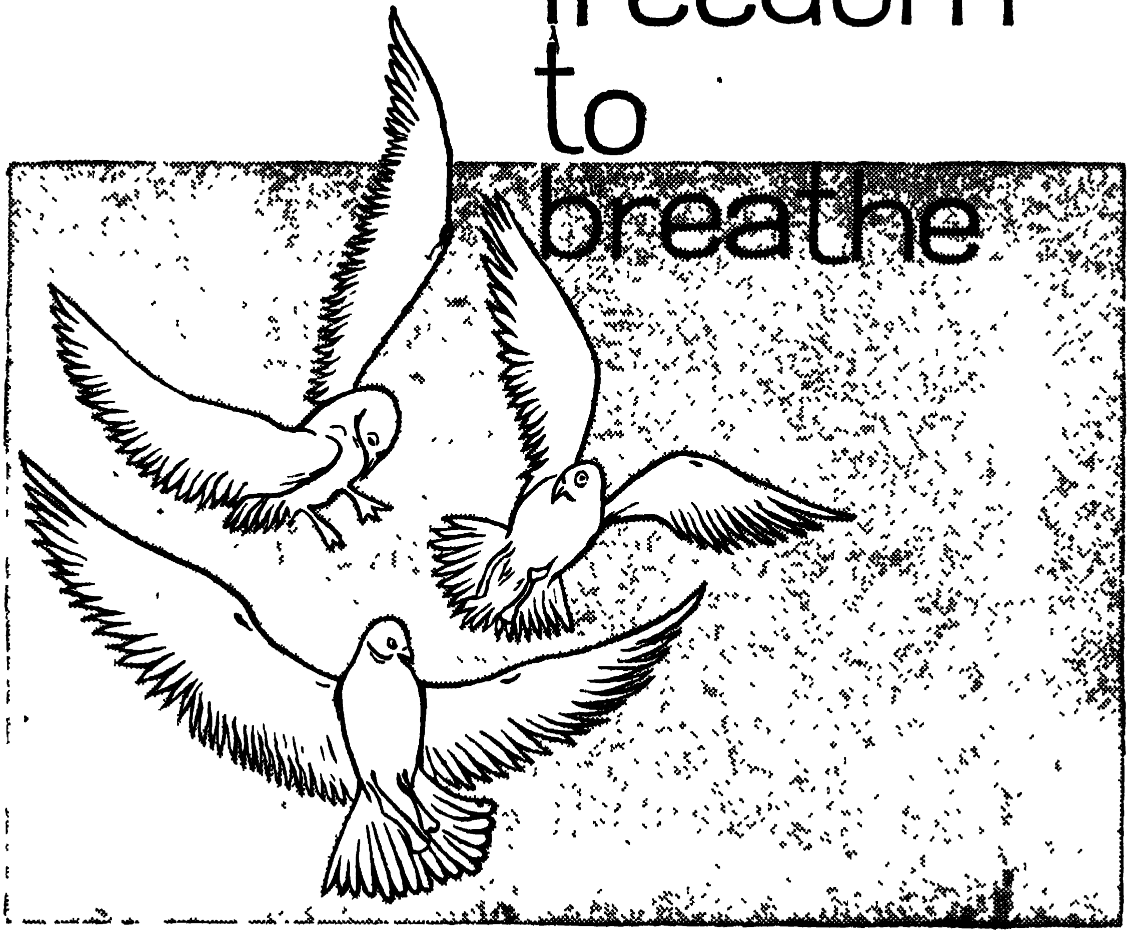

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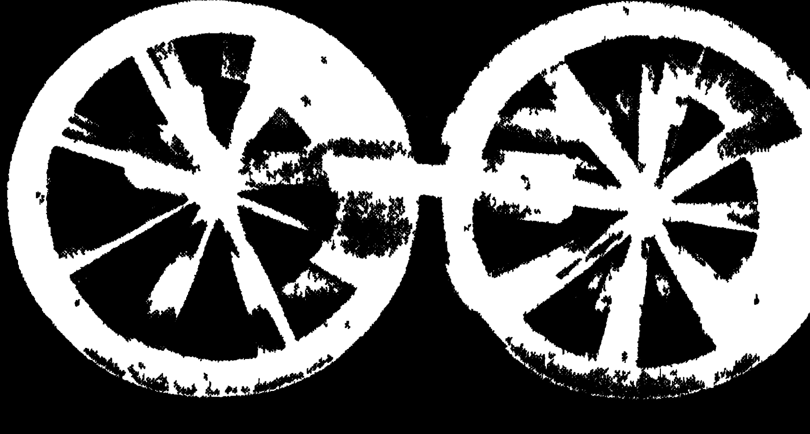

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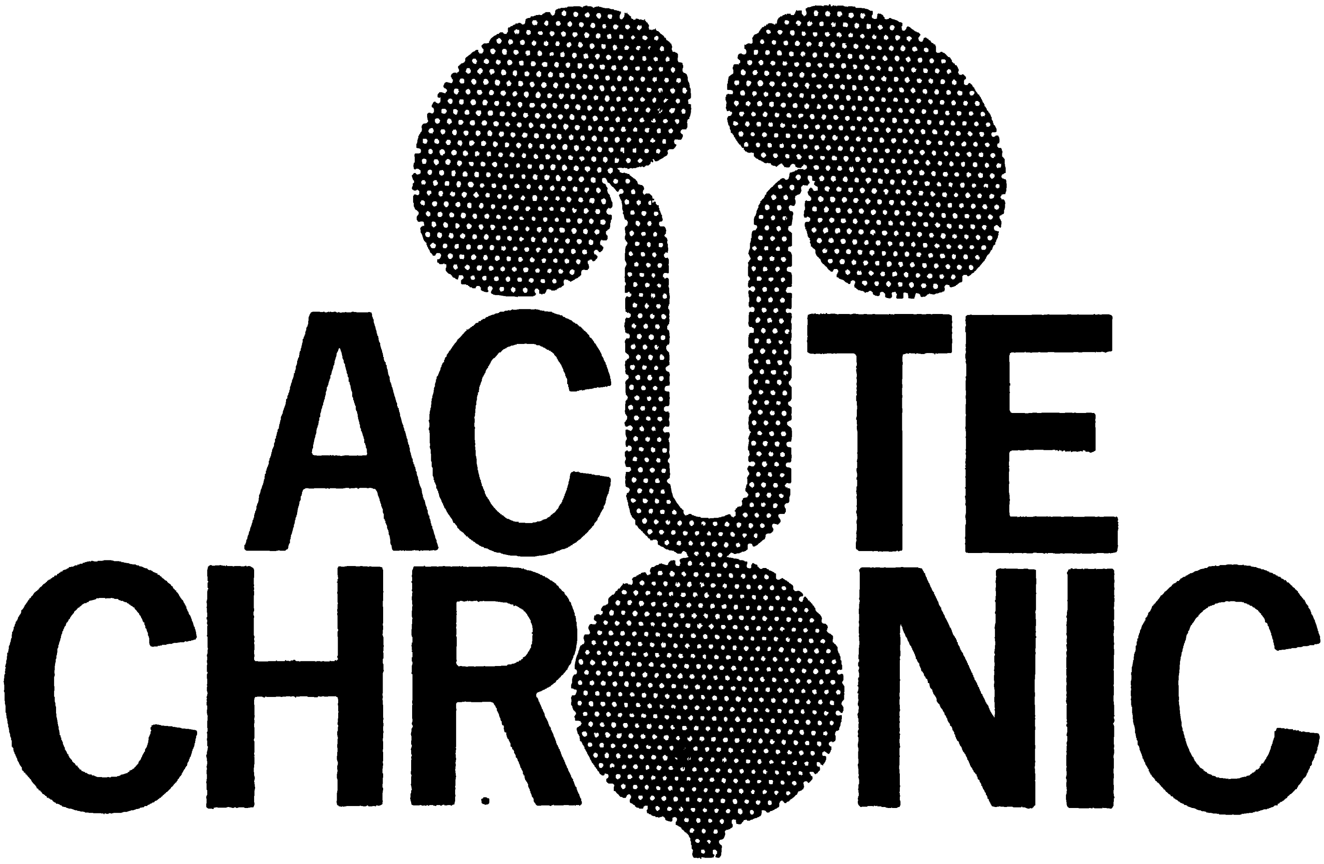

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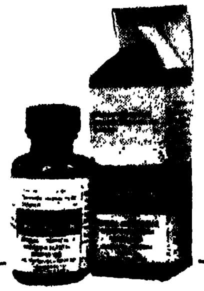

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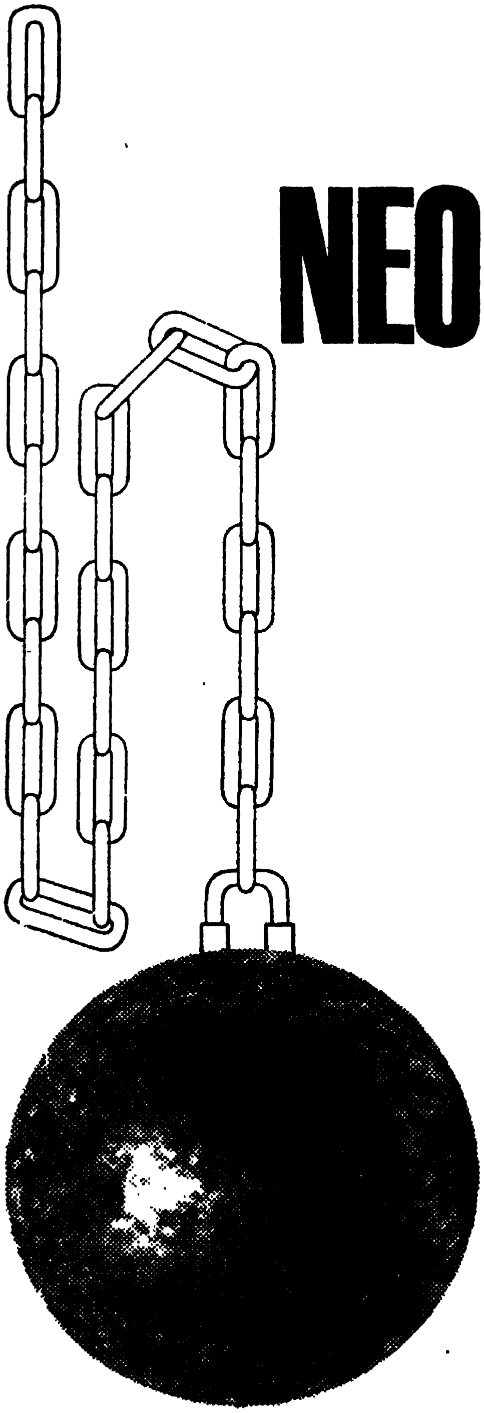

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Journal of the Indian Medical Association

VOLUME 45 — PUBLISHED TWICE A MONTH — OCTOBER 1, 1965
NUMBER 7 — EDITOR—N. BANERJEE, M.B. (CAL.), F.R.C.S. (ENG.), D.L.O. (LOND.) — CALCUTTA

ORIGINAL ARTICLES

SERUM LIPID LEVELS IN PHYSICALLY ACTIVE AND SEDENTARY SUBJECTS

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The preoccupation of the medical profession with the role of dietary factors in the regulation of serum cholesterol level has resulted in less attention being paid to other physiological factors regulating serum cholesterol level, e.g., stress and physical activity. During recent years, interest has been taken in these 'other physiological factors' and reports have appeared which indicate a negative correlation between the level of serum cholesterol and that of physical activity. A positive correlation has, however, been shown to occur between the level of serum cholesterol and that of mental stress and strain. The present investigation was undertaken to study the effect of physical activity and stress on the serum cholesterol and lipid phosphorus levels in clinically healthy subjects.

MATERIAL AND METHOD

The subjects of this investigation were adult males who belonged to low and middle income groups. Their monthly income ranged between Rs. 150/- and Rs. 300/-. The subjects belonged to two occupational classes, viz., one class was occupied in sedentary vocations, and the other class was occupied in jobs demanding heavy physical work. 200 subjects were investigated in each occupational class. Only those subjects were selected who were apparently and clinically healthy and who did not give family or personal history of any disease known to affect serum lipid level. Their age ranged between 20 and 40 years. Their height ranged between 4 ft. 8 inches and 5 ft. 9 inches, and their weight between 112 and 152 lb. The systolic blood pressure ranged between 116 and 130 mm. Hg and the diastolic between 74 and 86 mm. Hg.

Both classes of subjects lived in Mandiri, a municipal ward of Patna which is inhabited mostly by persons of low and middle income groups. The subjects of sedentary occupation were employed as clerks, school teachers, petty shopkeepers, etc. Those of physically active group were working as mechanics, blacksmiths, carpenters, hawkers, etc. A dietary survey of both the classes was carried out by the oral questionnaire method, as advocated by Padmavati *et al.* (1958) and Pasricha (1959).

Each day, four persons were taken up for investigations. Two ml. of venous blood was collected from each subject in the fasting state between 8 A.M. and 9 A.M. The blood was transferred to a conical centrifuge tube and the serum was separated by centrifuging the tube. The clear supernatant serum was decanted in a clean and perfectly dry test tube and was used for biochemical investigations. The serum cholesterol was determined by Sackett's modification of Bloor's method (Sackett, 1925). For determining the serum lipid phosphorus, the lipids were extracted into an alcohol-ether mixture and were digested with sulphuric acid and hydrogen peroxide as described by Youngberg and Youngberg (1930). The phosphorus now present as phosphate was then determined colorimetrically.

RESULTS

The dietary survey showed that the diet of these economically low and middle income groups of people was simple and monotonous with little variation. There was practically no difference in the food consumed by the sedentary and the physically active class of subjects. The average per head daily consumption of different food items was rice 8 oz., wheat flour 12 oz., pulses 4 oz., green and leafy vegetables 4 oz. and roots including potatoes 4 oz. Ninety-six per cent of the subjects were non-vegetarian, but the amount of meat or fish consumed by them was very small, for example, 2 to 4 oz. once or twice a week. They rarely consumed milk. The vegetable oil consumed daily was mustard oil at the level of 1 to 2 oz. per day. Ghee was a rare item and was consumed only on religious festivities. Vanaspati (hydrogenated vegetable fat) was a comparatively common item and was consumed at the level of ½ to 1 oz. daily.

Although the diet of both the classes of subjects were similar, the subjects differed markedly in the amount of physical acitivity taken and in the intensity of mental stress and strain to which they were subjected.

The nature of occupation of the sedentary subjects was such that physical exercise taken by them was negligible. They were intelligent people with high aspirations but were frustrated due to their low income as compared with that of persons well placed in life with equivalent education. Their low income in these economically hard times had made their lives miserable The combined effect of these factors was that they were in a stage of constant mental worry and anxiety.

On the other hand, the physically active subjects were employed in occupations which demanded heavy physical exercise. These subjects led an almost vegetative existence. They were interested in getting two square meals a day which were assured in this age of great demand for labour. Their wives and children also earned. Economically contented, with little ambition and with a firm faith in religion these subjects had much less mental worry and anxiety.

Table 1 gives the average figures and the range of serum cholesterol and lipid phosphorus level obtained in the sedentary and physically active subjects.

DISCUSSION

Table 1 shows that the serum cholesterol and lipid phosphorus levels are high in persons occupied in sedentary occupations than in persons occupied in physically active jobs. The physically active subjects were also those who had less mental stress and strain as compared to the sedentary subjects. The effect of physical activity on serum cholesterol level was studied by Gopalan and Ramnathan (1957) who showed that although the daily fat intake of both sepoys and army officers was 90 to 120 g., the serum cholesterol level of physically active sepoys was lower than that seen in sedentary army officers. Padmavati *et al.* (1961) showed in an epidemiological survey in Faridabad that the serum total cholesterol level was lowest in heavy workers. Gasell and Mayer (1962) showed that serum cholesterol level on fat intake was lower in physically active rural population of Blatten, a Swiss Alpine village, than in sedentary urban population of Basel, a Swiss town.

Besides sedentary life, increased mental stress and strain have also been shown to cause a rise in serum cholesterol level (Hammersten *et al.*, 1957; Wertlake *et al.*, 1958; Peterson *et al.*, 1962).

As the sedentary subjects of this investigation were also those who had more mental stress and strain than the physically active subjects it is difficult to say whether the raised serum cholesterol and lipid phosphorus levels in the sedentary subjects was due to less physical exertion or due to more stress and strain or due to a combination of both. In the above cited studies of Gopalan and Ramnathan (1957), Padmavati *et al.* (1958, 1961) and Gasell and Mayer (1962) it has probably been forgotton that the physically active subjects of their investigations belonged to such economic and occupational classes where mental stress and strain was much less as compared to their sedentary counterparts. It is, however, difficult in human beings to evaluate separately the effects of mental stress and strain and of physical activity on the serum lipid levels.

TABLE 1—SHOWING SERUM CHOLESTEROL AND SERUM LIPID PHOSPHORUS IN BOTH GROUPS OF SUBJECTS

Class		No. of subjects	Serum cholesterol (mg. %)		Serum lipid phosphorus (mg. %)	
			Average	Range	Average	Range
Sedentary	...	200	170·30±6·20	148·22 to 201·92	8·49±0·6	7·16 to 10·46
Physically active	...	200	134·42±5·50	112·84 to 153·10	7·97±0·8	6·68 to 10·24

SUMMARY

The serum cholesterol and lipid phosphorus levels have been studied in 400 normal healthy adult males of whom 200 were in sedentary occupations and the remaining 200 in physically active jobs. It has been found that those occupied in physically active jobs had lower serum cholesterol and lipid phosphorus levels.

ACKNOWLEDGMENT

The work was carried out at the Postgraduate Department of Physiology, P. W. Medical College, Patna, under Prof. A. S. Sinha to whom the author is greatly obliged.

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A CONTROLLED TRIAL OF PREDNISOLONE IN THE TREATMENT OF INFECTIVE HEPATITIS*

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Value of corticosteroids in the treatment of infective hepatitis is still the subject of dispute. Evans *et al.* (1953), Ducci and Katz (1955), Ducci *et al.* (1957), Kirkeby *et al.* (1955) and others reported rapid symptomatic improvement and accelerated fall in serum bilirubin levels in patients treated with corticosteroids. Johnson and Bennett (1955) concluded that A.C.T.H. is ineffective in the treatment of a routine case of infective hepatitis. The opinion is widely divided whether corticosteroids shorten the duration of the illness and accelerate the rate of biochemical and histological recovery. Early workers (Heilmeyer *et al.*, quoted by Ducci *et al.*, *loc. cit.*; Evans *et al.*, *loc. cit.*; Huber and Willey, 1955) were impressed that the steroid therapy shortens the duration of the illness but this was not the experience of later workers (Ducci *et al.*, *loc. cit.*). Johnson and Bennett (*loc. cit.*) observed a more rapid reversion of flocculation tests to normal whereas Ducci *et al.* (*loc. cit.*) and Naglo *et al.* (1959) did not find any significant differences in return of flocculation tests or alkaline phosphatase with steroid therapy. Naglo *et al.* (*loc. cit.*) found that the time taken for serum bilirubin and bromsulphalein retention to return to normal was not significantly different between controls and patients treated with steroids. Reported rate of fall of serum bilirubin with steroids varies from 21 per cent to 60 per cent. Sborov *et al.* (1954) found no difference in liver biopsies of cases of hepatitis treated with steroids whereas Evans *et al.* (*loc. cit.*) reported a rapid healing of histological lesions.

In view of these divergent opinions, a controlled trial with prednisolone in viral hepatitis was felt necessary to assess its value on clinical, biochemical and histological recovery.

MATERIAL AND METHOD

All cases of viral hepatitis admitted to the Medical Unit 1 between January 1961 and October 1963 have been included except those which left hospital against advice. In all 57 cases are reported.

Alternate cases were given prednisolone. Alteration was done typewise except cases with coma which were treated with prednisolone.

Diagnosis has been based on clinical and histopathological evidence in 47 cases, in the remaining 10 on clinical and biochemical evidences. Cases were arbitrarily classified into three clinical types depending on serum bilirubin on admission (mild—serum bilirubin <8 mg. per cent; moderate —serum bilirubin >8 mg. but <16 mg. per cent; severe—serum bilirubin >16 mg. per cent) and in three histological grades (grades I, II and III) depending on the amount of portal tract infiltration, cellular degeneration and necrosis of liver cells.

---

* Read at the First Asian Congress of Gastroenterology, Chandigarh, January 1964

Both the groups received full hospital diet (protein 70 g., fat 70 g., calories 2000) and were given *ad lib* bed rest. Patients in the treated group received 10 mg. prednisolone four times a day. The dose was reduced to 30 mg. per day in the second week, 15 mg. per day in the third week and tapered thereafter when serum bilirubin became 1·5 mg. per cent. Hepatic coma cases received equivalent doses of hydrocortisone intravenously till oral medication was possible. Intravenous glucose was administered only when vomiting was a serious problem.

Serum bilirubin, alkaline phosphatase, thymol turbidity, serum transaminase estimations were done initially and every 3rd to 5th day subsequently. Where possible, serial liver biopsies were done every 8th to 10th day. In 18 cases, three or more serial biopsies were done ; in 13 cases two biopsies and in 16 cases only one initial biopsy was possible. Various types of viral hepatitis studied are shown in Table 1.

TABLE 1—SHOWING TYPES OF VIRAL HEPATITIS STUDIED

Type of hepatitis	No. of cases Prednisolone group	Control group
(1) Acute hepatitis	22	19
(2) Hepatitis with precoma ...	5	—
(3) Subacute hepatitis	2	2
(4) Cholestatic hepatitis		
Obstructive type (Smatena, 1957)	2	2
Cholangiolytic type (Watson and Hoffbauer, 1946) ...	3	—
Total	34	23

Comparability of the two groups—Table 2 shows that the two groups of acute viral hepatitis are comparable with respect to various criteria.

Criteria for evaluation of the treatment—Results of the treatment have been assessed by several criteria (Table 3) as follows :

1. Clinical assessment—Number of days required for : (a) Temperature to return to normal. (b) The return of feeling of well-being, appetite and for disappearance of nausea and vomiting. (c) The regresion of liver size and tenderness.

2. Biochemical assessment—(a) Serial estimations of serum bilirubin: (i) rate of fall. (ii) time taken to return to 50 per cent level and to 1·5 mg. per cent. (b) Serial estimation of alkaline phosphatase, serum transaminase and thymol turbidity.

TABLE 2—SHOWING COMPARABILITY OF THE TWO GROUPS OF ACUTE HEPATITIS (STANDARD TYPE)

Criteria	Prednisolone group	Control group
No. of cases	21	19
Mean age (years)	25·8	31·4
Sex :		
No. of males	16	15
No. of females	5	4
Mean period of disease before acceptance to trial (days)	7·9	8·3
Intercurrent diseases (No. of cases) :		
Pregnancy	1	1
Diarrhoeas, dysenteries	2	2
General health and nutrition (No. of cases) :		
Good	6	5
Fair	15	14
Severity of jaundice on admission (No. of cases) :		
(a) Mild serum bilirubin up to 6 mg. per cent	5	6
(b) Moderate serum bilirubin 6 to 12 mg. per cent	8	8
(c) Severe serum bilirubin above 12 mg. per cent	7	5
Mean serum bilirubin (mg. per cent) (on admission)	8·69	10·18
Mean alkaline phosphatase (K. A. units) (on admission)	17·98	15·89
Mean thymol turbidity (units) (on admission)	5·25	6·58
Histological grading of cases :		
Grade I	6	5
Grade II	8	8
Grade III	3	3
Grade nil	4	3

3. Duration of disease—Judged from the time required for serum bilirubin to return to 1·5 mg. per cent after acceptance to the trial.

4. Complications—(a) Incidence of recrudescence. (b) Side effects of treatment.

5. Histological assessment—From serial liver biopsies.

RESULTS

1. *Acute infective hepatitis*—The following features were observed in the treated group on comparison with the control group.

(a) Rapid subjective improvement : The general condition and appetite improved earlier in the treated group. The average period for subjective improvement after initiation of trial was 5 days for the treated group against 9 days for the controls. The rate of improvement of subjective

TABLE 3—SHOWING RESULTS UNDER VARIOUS CRITERIA IN TREATED AND CONTROL GROUPS

Criteria	Average No. of days required	
	Prednisolone group	Control group
Return of feeling of well-being and appetite ...	5	9
Return of temperature ...	3 (7/21)	4½ (8/19)
Disappearance of nausea and vomiting ...	4	7·5
Disappearance of liver tenderness	13·66	12·68
Disappearance of liver enlargement	20·3 (12/21)	23·78 (9/19)
Fall of serum bilirubin to 50%	5·1	8·18
Fall of serum bilirubin to 1·5 mg. %	18·59	19·69
Average weight loss at the time of discharge ...	1 kg. (11/21) (10 cases, no loss)	2·5 kg.

symptoms like nausea, vomiting, malaise and disturbance of sleep was more rapid in the treated group. However, no difference was found as far as pruritus and diminution of liver size were concerned. Ten and nine patients of control and treated groups respectively had palpable liver at the end of the trial period (i.e., serum bilirubin 1·5 mg. per cent). At the time of discharge, more than half of the treated patients had regained their original weight, the rest showed an average weight loss of 1 kg. against an average loss of 2·5 kg. for the controls.

(b) Improvement in bilirubinaemia: There was a rapid clearance of bilirubin from the blood in the treated group. Mean serum bilirubin concentration of patients on admission and on third, sixth, ninth and twelfth day of admission in the two groups are shown in Table 4.

Table 4 shows that the mean serum bilirubin in treated group is considerably lower on 3rd, 6th and 9th day as compared to the respective means for the controls; however, these differences are not statistically significant as the observed differences are about 1·5 times its standard error. The differences between the groups narrow down on the 12th day. After twelve days, the mean levels of both the groups run parallel with a very slight advantage in favour of the treated group. The fall of serum bilirubin in prednisolone treated patients is abrupt and of bigger magnitude in the first three days as compared to the rest of the clinical course of the disease. The control group shows a steady fall spread over the whole duration.

Average period for bilirubin to fall to 50 per cent level in treated group was 5·1 days against 8·18 days for the controls. However, the mean period for serum bilirubin to fall to 1·5 mg. per cent was found to be almost equal, viz., 19·69 days for the cantrols against 18·59 days for the treated group. Thus, it can be concluded that the rate of bilirubin clearance is rapid with prednisolone therapy initially but tends to be gradual later on and the total period required for return to normal is more or less the same for both the groups.

(c) Improvement of other biochemical tests: Mean values of alkaline phosphatase, serum transaminases and thymol turbidity, on admission, on 6th and 12th day of the trial in both the groups are shown in Table 5. There is no significant difference between the two groups in the rate of fall of these tests.

(d) Duration of the disease: As judged by the number of days required for serum bilirubin to fall to 1·5 mg. per cent the mean duration of the disease was comparable in both the groups, viz., 18·59 days for the treated against 19·69 days for the control group. One case of recrudescence has been excluded from this consideration; otherwise the duration of the disease for the treated group would work out to be longer than that of the controls.

TABLE 4—SHOWING MEAN SERUM BILIRUBIN AND PERCENTAGE FALL OF SERUM BILIRUBIN AT VARIOUS INTERVALS

Group	Mean serum bilirubin (mg. per cent) and percentage fall									Days required for serum bilirubin to fall to	
	On admission	3rd day		6th day		9th day		12th day			
	mg. %	mg. %	fall %	mg. %	fall %	mg. %	fall %	mg. %	fall %	50%	1·5 mg. %
Prednisolone ...	8·6	5·7	34	4·2	49·2	3·5	59·6	2·9	68·1	5·1	18·59
Control ...	10·1	8	21·3	6·7	35	5	50·6	3·5	65	8·1	19·69

TABLE 5—SHOWING MEAN OF VARIOUS LIVER FUNCTION TESTS IN TWO GROUPS OF ACUTE INFECTIVE HEPATITIS (STANDARD TYPE) AT VARIOUS INTERVALS

Liver function tests	Group	On admission	On 6th day	On 12th day
Alkaline phosphatase (K.A. units)	Control	15·89	11·62	10·26
	Prednisolone	17·98	14·98	12·91
Thymol turbidity (units)	Control	6·5	6·0	5·8
	Prednisolone	5·2	4·8	4·1
S.G.O.T. (units)	Control	317	220	144
	Prednisolone	321	149	99
S.G.P.T. (units)	Control	363	248	171
	Prednisolone	332	200	130

(c) Incidence of recrudescences: Recrudescences are considered as those instances in which bilirubinaemia increases after having fallen to 1·5 mg. per cent. There was one case of recrudescence in the prednisolone group.

The recrudescence occurred after 8 days of discontinuation of prednisolone. It was associated with recurrence of manifestations and increase in serum bilirubin necessitating second course of prednisolone. In the control group, there was no incidence of recrudescence.

(f) Histological improvement. Serial liver biopsies were available in 12 controls and 10 treated cases; in 6 controls and 5 treated cases, three or more biopsies were available and in the rest only two.

Serial biopsies were assessed by the pathologist without prior knowledge of treatment group. The improvement in serial slides was rated by comparing the quantity of portal tract infiltration, cellular degeneration and necrosis. The attempt at quantitative evaluation of improvement numerically was abandoned due to inherent difficulties. Histological improvement was compared in both the groups gradewise and it was felt that the rate of improvement in individual grades in both the groups was more or less similar.

The histological improvement was also studied by comparing the final slides (i.e., when serum bilirubin had dropped to 1·5 mg. per cent) of the patients of both the groups. The histological picture was comparable in both the groups. Considerable amount of inflammation was present in all the slides suggesting histological improvement followed clinical and biochemical recovery. None of the liver biopsies of the treated cases showed fatty infiltration.

The conclusion of the study is that histopathology of both groups show similar variability and run more or less the same course.

2. *Hepatitis with precoma*—There were 5 patients of hepatitis with signs of precoma. All the cases of this group were treated with prednisolone. One case died within two days and another died after 8 days; the rest of the three cases made uneventful recovery. In the three cases that survived, liver biopsies were done 8 to 10 days after clearing of the coma and were found to be of standard type (acute hepatitis) grade I (one case) and grade II (2 cases). The course of the disease in these three cases was similar to that observed in treated cases of acute type and hence the details are not repeated.

3. *Cholestatic hepatitis*—There were seven cases of cholestatic hepatitis. 4 of these were of the 'obstructive' type of Smatena (*loc. cit.*) and 3 of 'cholangiolytic' type of Watson and Hoffbauer (*loc. cit.*).

In the obstructive type 2 were treated with prednisolone and the rest served as controls. The clinical, and biochemical and histological improvement in these groups was similar (Table 6).

All the three patients of the cholangiolytic type of Watson were treated with prednisolone. The details of these three cases are given in Table 6.

Though subjective improvement was present in all the three cases, substantial fall in serum bilirubin was noted only in one case. Of the remaining 3 cases of this type, the serum bilirubin came to normal in 45 days in one case and 20 days of prednisolone therapy had no influence on the bilirubin level in the other. Serial biopsies of these cases showed that the rate of improvement was at a much slower pace when compared to acute hepatitis—standard type.

4. *Subacute hepatitis*—Of the 4 cases with histological picture of subacute hepatitis, two were treated with prednisolone, the other two served as controls. One patient in each group took 30 and 60 days respectively before serum bilirubin showed remission to 1·5 mg. per cent. Subjectively, treated cases felt better earlier and returned to normality faster than controls. No significant difference was observed in time for bilirubin or for other liver function tests to return to normal. Histopathological study showed that improvement was minimal in both the groups in spite of clinical and biochemical improvement.

Complications and side effects of prednisolone therapy: Mention has already been made of one case of recrudescence of jaundice among the treated group. Five patients receiving prednisolone developed heartburns and two developed moon face

TABLE 6—SHOWING DETAILS OF CHOLESTATIC HEPATITIS

Case No.	Treatment group	Duration of illness prior to biopsy (days)	Serum bilirubin mg. %				Alkaline phosphatase (K.A. units)			S.G.O.T./ S.G.P.T. (units)			Thymol turbidity (units)			Days for serum bilirubin to become		Days for clinica improvement
			On admission	3rd day	9th day	12th day	On admission	6th day	12th day	On admission	6th day	12th day	On admission	6th day	12th day	50 %	1·5 mg. %	
									OBSTRUCTIVE TYPE									
9	P	9	4·1	9·1	3·9	5·0	16·7	14 2	15·6	460/ 510	170/ 190	230/ 290	2	7	4	6	16	5
28	C	8	6·1	4·5	2·6	2·3	8·2	9·3	6·0	90/ 250	40/ 150	50/ 170	14	10	6	6	20	6
32	P	5	5·7	3·5	1·8	1·5	25	13	18·7	...	...	...	3	5	4	7	12	7
56	C	7	4·9	4·0	2·5	1·8	16·6	13	13·9	140/ 320	150/ 250	150/ 250	6	5	6	9	15	7
									CHOLANGIOLYTIC TYPE									
38	P	10	25·2	25·2	12·1	10·3	25·2	22·9	18·2	80/ 120	60/ 100	150/ 200	5	6	3	9	43	8
40	P	90	12·8	12·0	11·3	11·4	22	19	26	140/ 300	180/ 350	170/ 380	3	3	3	Did not come down in 20 days' treatment		10
61	P	60	13·2	8·1	2·9	1·8	24·2	16·4	14·8	390/ 520	200/ 350	120/ 190	4	5	4	6	14	6

N.B.— C = Control. P = Prednisolone.

and acne all over the body. The reactions cleared up on discontinuation of the therapy.

DISCUSSION

Evaluation of any drug in the treatment of infective hepatitis is difficult as it is a variable disease. There are many clinical types having a variable course and prognosis. Diagnosis of these types can only be made with certainty by liver biopsy examination. A clinical trial without liver biopsy control is likely to be misleading as various types may be disproportionately distributed in the treated and control groups.

From the data given above, it appears that the use of prednisolone brings a rapid and remarkable subjective improvement associated with a rapid initial fall of serum bilirubin. The fall in serum bilirubin is most marked in the first three days and becomes progressively decreased so that serum bilirubin levels in treated and control groups tend to be equal after the second week. The subjective improvement and rapid rate of clearance of serum bilirubin is not associated with improvement in other liver function tests nor with shortening of the duration of the disease. The mechanism of the rapid fall of serum bilirubin with steroid therapy is not clearly understood. The concomitant histological study does not suggest that the symptomatic improvement and fall in serum bilirubin is due to regression of the lesion.

Different workers have reported variable percentage fall of serum bilirubin with corticosteroid therapy. Variability of the disease and differences in clinical material explain, to a certain extent, these differences. Several authors have commented on the high incidence of relapses in prednisolone treated cases. It is suggested that the relapses are infrequent if gradually tapered dose is continued well into convalescence. In the present series, there was one instance of recrudescence (5 per cent) in spite of observing this precaution. Long-term therapy of steroids has its own disadvantages and may lead to minor or major side effects.

Routine use of steroid therapy in management of acute benign hepatitis is not justified when the duration of the disease is not shortened and the histopathological recovery is not hastened.

Nelson (1957) has concluded that the use of steroids is justified in severe forms of the disease. Ducci and Katz (1952) have shown the value of high dose of steroids in fulminant hepatitis. Two of our cases of precoma deepened into coma and died. Dose employed in these cases was much smaller than that used by Ducci and Katz (1952). All cases of hepatitis in coma are not examples of fulminant hepatitis. Cases of acute hepatitis may also go into hepatic coma without having gross pathological disturbances of fulminant hepatitis. These have better prognosis than fulminant hepatitis. Such cases should not be mixed up with the latter in assessment of therapy.

In the present series, two types of cholestatic hepatitis were seen. In four cases, marked cholestasis was seen from the beginning of the disease and the histological picture resembled that described by Smatena (*loc. cit.*). These cases behave almost like acute benign hepatitis and the influence of prednisolone in this group was similar to that in benign hepatitis. In other 3 cases, cholestasis was prolonged and histology resembled that described by Watson and Hoffbauer (*loc. cit.*). In two of these three cases there was no spectacular improvement with prednisolone. Johnson *et al.* (1956) and Sheldon (1957) have reported prompt fall in serum bilirubin and shortening of the duration of the illness in this variety.

Value of steroids in subacute and chronic hepatitis remains to be proved. Use of steroid in subacute hepatitis is helpful in producing symptomatic relief and clearing of jaundice but does not seem to change the course of the disease.

The high incidence of cholestatic hepatitis in the present series may be a source of surprise to many. A similar incidence was also noted during the Delhi epidemic where many patients were subjected to biopsy examination. This variety could be detected more frequently if biopsies are scrutinised more carefully for evidence of cholestasis. Some of bile retention is also a feature of the standard type of infective hepatitis, in the early and subsiding phases and need to be differentiated from true cholestatic hepatitis.

SUMMARY

A controlled trial of prednisolone in the treatment of various types of infective hepatitis is reported. In all, there were 57 cases consisting of 41 acute benign hepatitis, 5 hepatitis with precoma, 7 cholestatic hepatitis and 4 cases of subacute hepatitis. Twenty-two of the acute benign hepatitis, 5 of the hepatitis with precoma, 5 of the cholestatic and 2 of subacute hepatitis have been treated with prednisolone, the rest served as controls. The two groups of acute hepatitis were comparable.

The present trial suggests that prednisolone causes an initial rapid fall in serum bilirubin level, improvement in appetite and rapid return of feeling of well being and gain in weight. It has no influence on vomiting or histopathological progress and does not shorten the duration of the disease. Rate of fall of serum bilirubin levels of treated and control groups tends to be equal after 12 days of therapy. The treatment is accompanied with the increased risk of recrudescence and danger of side effects. Steroid therapy is useful in severe hepatitis in precoma. In none of the types, steroid therapy had any influence on the disease process as judged from histology. The routine steroid treatment of acute benign hepatitis does not seem beneficial. The drug is a useful weapon in selected cases of severe hepatitis.

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FOLIC ACID ESTIMATION IN NORMAL SUBJECTS AND IN MEGALOBLASTIC ANAEMIA CASES*

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There are various conflicting reports about the deficiency of folic acid and vitamin B_{12} in cases of nutritional macrocytic anaemia.

Das Gupta *et al.* (1953) on the basis of therapeutic response thought that the major and primary deficiency in tropical macrocytic anaemia was of folic acid. Gupta and Gupta (1953-54) also

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* This work was supported by I.C.M.R. grant during the year 1962-63.

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reported the same findings. On the other hand, Patel (1948) on the basis of therapeutic responses and Baker (1958) on the basis of vitamin B_{12} assays and radioactive vitamin B_{12} absorption studies found vitamin B_{12} deficiency in majority of cases. Chatterjea (1958) reported folic acid as a major deficiency in nutritional megaloblastic anaemia.

There are scanty reports about serum folic acid level in cases of anaemia in India. Chatterjea (1958) reported that serum folic acid levels as measured with *Streptococcus faecalis* R as test organism varied widely and did not represent any pattern significantly different from those in control groups. Recently as this work was under publication, Banerjee and Chatterjea (1964) reported serum folate levels of 3·0 to 22 mμg. in normal Bengalees, in nutritional macrocytic anaemia with megaloblastic marrow, the range was distinctly low and varied from 0·5 to 2·3 mμg. per ml. of serum.

In other countries Witts (1956), Chanarian (1958) and Luhby (1959) have reported that folic acid nutritional status of man could not be assessed by whole blood or serum sampling. Herbert (1961) has shown by employing his technique, that serum folic acid activity can be measured satisfactorily, and it correlated well with the diagnosis based upon therapeutic response in cases of anaemia due to various causes. Walters and Mollin (1961) also confirmed it.

It was therefore thought desirable to estimate folic acid in normal and macrocytic anaemia by the new technique of Herbert (1961).

MATERIAL AND METHOD

Herbert's (1961) method for folic acid estimation was followed except with certain modifications. In the beginning, vitamin-free acid hydrolysate casein (Difco) was used, as vitamin-free salt gave a precipitate on autoclaving which did not disappear on cooling. Otherwise, it gave satisfactory results. B.B.L. dry mix medium was also used. It was satisfactory but gave slight turbidity on heating. The dry mix media prepared by Difco Lab according to Walters and Mollin's modification (1961) were tried, and they proved to be very satisfactory. L. Casei (A.T.C.C. no. 7469) was used as a test organism. All glassware were rendered folic acid free by washing first in potassium dichromate sulphuric acid, and subsequently washing them 6 times with double distilled water.

The preparation of serum samples and assay protocol was the same as of Herbert (1961). But the method of inoculation was as suggested by Walters and Mollins (1961) because the carry over of folic acid in the method of Herbert is considerable. The ascorbic acid concentration, 100 mg. per 100 ml., was used. In the method of Herbert (1961), the ascorbic acid protects the heat labile folic acid. This is the main advantage over other methods. Vitamin B_{12} estimation was done by the method of Mollin and Ross (1962) using Euglena gracilis "z" strain.

The xylose absorption and serum carotene were also carried out.

These investigations were done in normal control groups having no gastro-intestinal disturbances, but with normal haematological values. In the control group, there were two subgroups, one having people belonging to villages, the other subgroup consisted of people of good social status, such as medical students, doctors, etc. This subdivision of control group was necessary as patients with anaemia usually belonged to villages, were poor, and were fed on poor diet. The division of normal control into two groups, such as vegetarian and non-vegetarian, was made according to dietary habits. The vegetarian group usually took vegetable proteins and only occasionally consumed animal proteins.

The anaemic patients were selected on the basis that they were not cases of secondary type, due to some disease, and in these cases dimorphic anaemia, megaloblastic anaemia cases were grouped separately.

Haematological examination showed the following main findings:

(a) *Megaloblastic anaemia cases*:

Bone marrow reaction—Megaloblastic.

Haemoglobin—Mean value was 9·1 g. per cent and the range varied from 4 to 11·5 g. per cent.

P.C.V.—Mean value was 42·5 per cent and range varied from 35 to 50 per cent.

The red blood cells showed slight macrocytosis and hypochromia.

W.B.C.—The counts were normal. Some of the polymorphs showed macropolycytosis, and other leucocytes were normal.

Platelets—The platelet count was normal.

(b) *Dimorphic anaemia cases*:

Bone marrow reaction—Both megaloblastic and normoblastic.

Haemoglobin—Mean value was 7·5 g. per cent and the range varied from 3·5 to 11 g. per cent.

P.C.V.—Mean value was 30 per cent and the range varied from 25 to 34 per cent.

W.B.C.—The count was normal. The leucocytes were normal.

The red blood cells showed both microcytosis and macrocytosis and hypochromia.

The platelet count was normal.

Blood protein levels in both cases were normal.

TABLE 1—SHOWING FOLIC ACID AND VITAMIN B_{12} VALUES IN DIFFERENT OBSERVATIONS

Items	Range	Mean	No. of cases
	NORMAL INDIVIDUALS IN LOW INCOME GROUP		
Folic acid	4·0 to 8·5 mμg.	6·05 mμg.	30
Vitamin B_{12}	150 to 575 $\mu\mu$g.	341 $\mu\mu$g.	30
	NORMAL INDIVIDUALS WITH GOOD SOCIO-ECONOMIC STATUS		
Folic acid	3·5 to 11 mμg.	7·68 mμg.	30
Vitamin B_{12}	180 to 625 $\mu\mu$g.	580·5 $\mu\mu$g.	30
	MEGALOBLASTIC ANAEMIA CASES		
Folic acid	0·2 to 2·2 mμg.	0·91 mμg.	25
Vitamin B_{12}	103 to 270 $\mu\mu$g.	179·6 $\mu\mu$g.	25
	DIMORPHIC ANAEMIA CASES		
Folic acid	0·6 to 2·5 mμg.	1·2 mμg.	20
Vitamin B_{12}	175 to 290 $\mu\mu$g.	219 $\mu\mu$g.	20
	OTHER ANAEMIA CASES		
Folic acid	0·78 to 3·7 mμg.	1·24 mμg.	10
Vitamin B_{12}	110 to 225 $\mu\mu$g.	183·5 $\mu\mu$g.	10
	VEGETARIANS		
Folic acid	4·00 to 11 mμg.	6·9 mμg.	48
Vitamin B_{12}	150 to 450 $\mu\mu$g.	326·9 $\mu\mu$g.	48
	NON-VEGETARIANS		
Folic acid	5·9 to 10 mμg.	7·86 mμg.	12
Vitamin B_{12}	215 to 612 $\mu\mu$g.	434·3 $\mu\mu$g.	12

TABLE 2 SHOWING XYLOSE ABSORPTION

Total cases of anaemia ...	25
Value below 20 per cent ..	6

TABLE 3—SHOWING FAECAL FAT

Normal range— 2 to 5 g. per cent
Range—7 to 32 g. per cent in 6 cases
Total No. of cases—25

DISCUSSION

It can be seen from Table 1 that folic acid levels in the people belonging to villages is 6·05 milli-micrograms, with a range of 4·0 to 8·5 milli-micrograms per ml. In persons with good social status and good diet it ranged from 3·5 to 11 milli-micrograms per ml., with a mean of 7·68 milli-micrograms compared to the folic acid levels of 5·9 to 21·0 milli-micrograms per ml. obtained by Walters and Mollins (1961). Using this new method of folic acid estimation it is quite apparent that the levels of folic acid in an average Indian in this part of Rajasthan are apparently lower than those obtained in U.K. Here the individuals apparently normal are just on the border line of lower limit of normal level, as reported by Walters and Mollin (1961).

Patients having megaloblastic and dimorphic anaemias showed considerable low levels of folic acid (Table 1). There was no significant difference in folic acid levels in the vegetarian and non-vegetarian groups.

Thus a satisfactory method based on the newer technique was established for the estimation of folic acid. These values are considerably lower than those reported by Chatterjea (1958) and Satoskar *et al.* (1961). They are possibly values more near the correct figure, in view of the unsuitability of *Strept. faecalis* as the test organism, which was used in studies referred to above. With this technique of folic acid estimation in the blood, the deficiency of folic acid can easily be diagnosed.

Vitamin B_{12} levels were slightly lower in cases of anaemia as compared to the levels in normal cases (Table 1).

It is also clear from Tables 2 and 3 that some of the patients had marked fat excretion in stools, while others had low xylose absorption values. This indicated that a few cases of megaloblastic anaemias suffer from malabsorption.

SUMMARY AND CONCLUSION

A method for satisfactory laboratory estimation of folic acid has been established.

The normal average values by this method have been found to be 6·05 milli-micrograms per ml. In case of anaemias, the range of folic acid was 0·2 to 2·2 milli-micrograms per ml. Vitamin B_{12} assays reveal normal average levels of 341 micro-micrograms per ml. and in average anaemia cases it was 179·6 micro-micrograms per ml.

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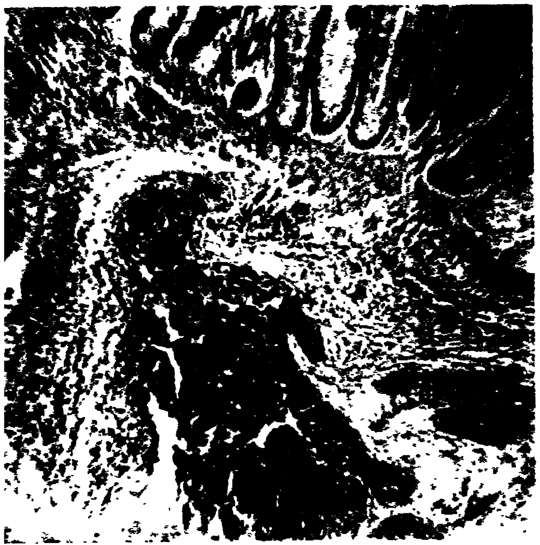


Fig. 2

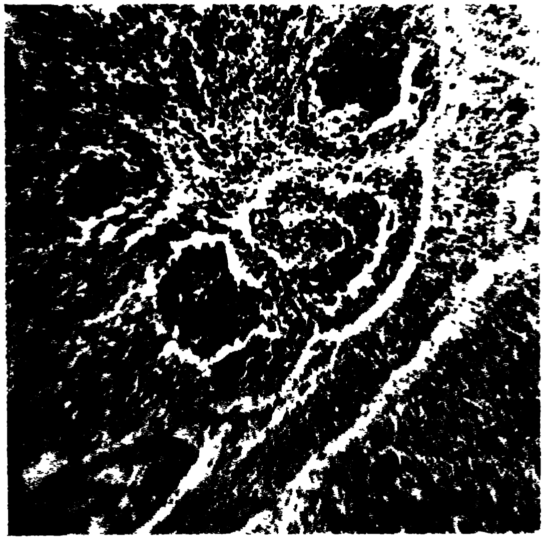
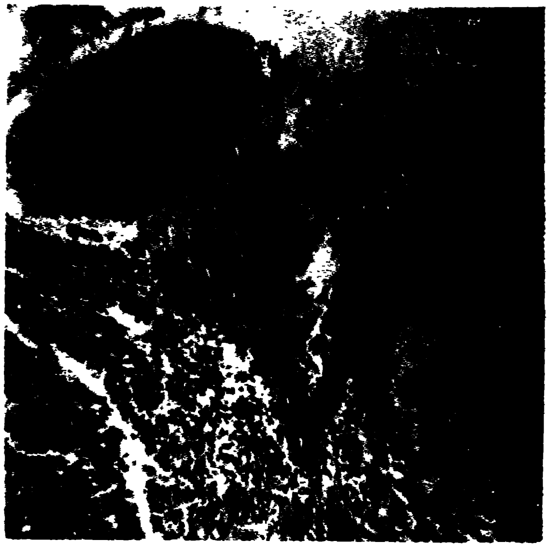


Fig. 3



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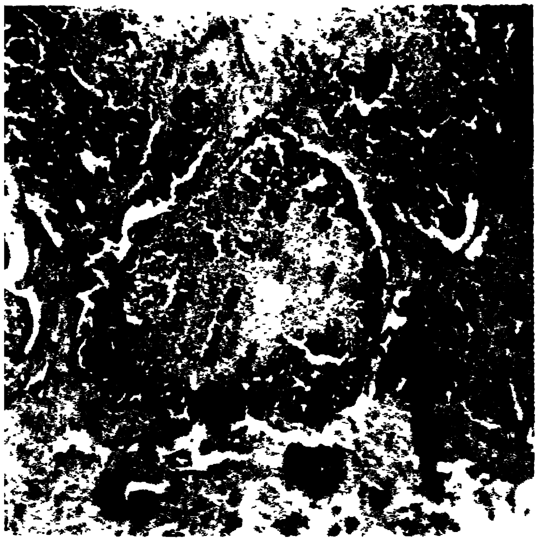

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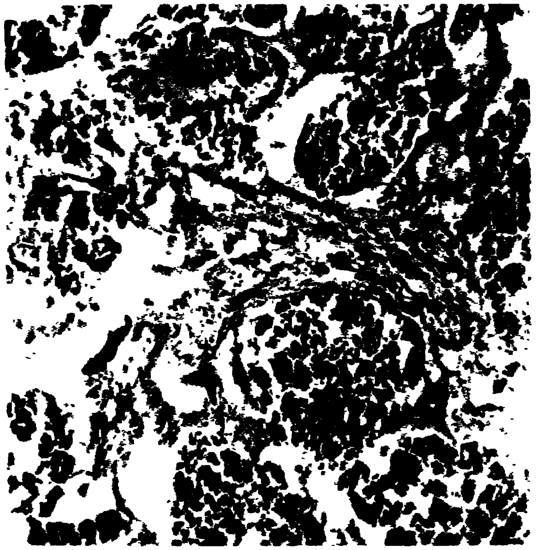

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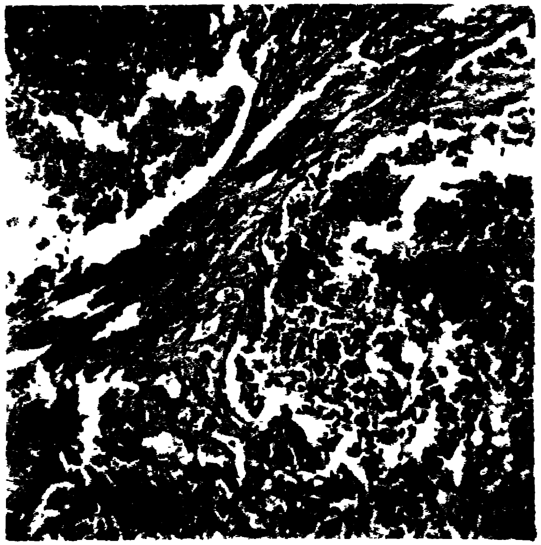


Fig. 7

Sanyal—Treatment of a Case of Cancer with m-Xylohydroquinone (P. 369)

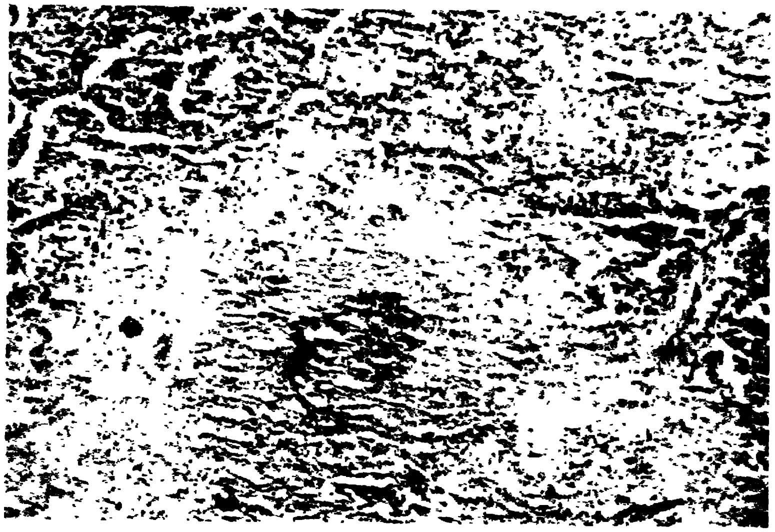
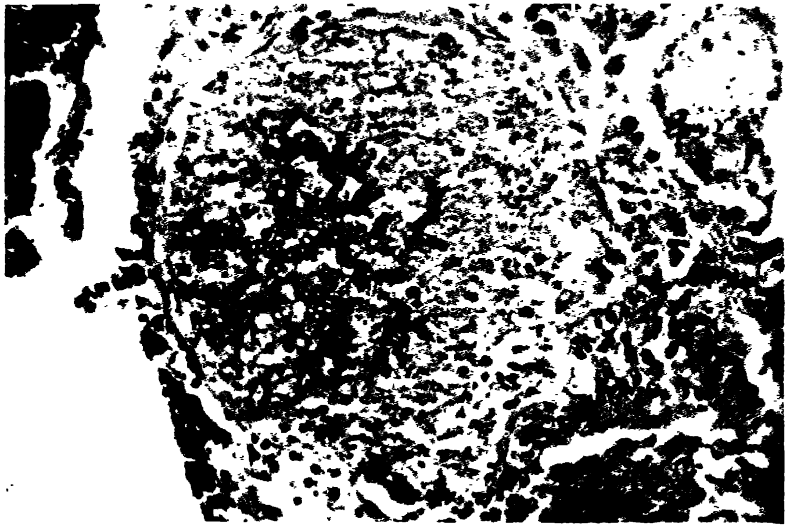


Fig. 1



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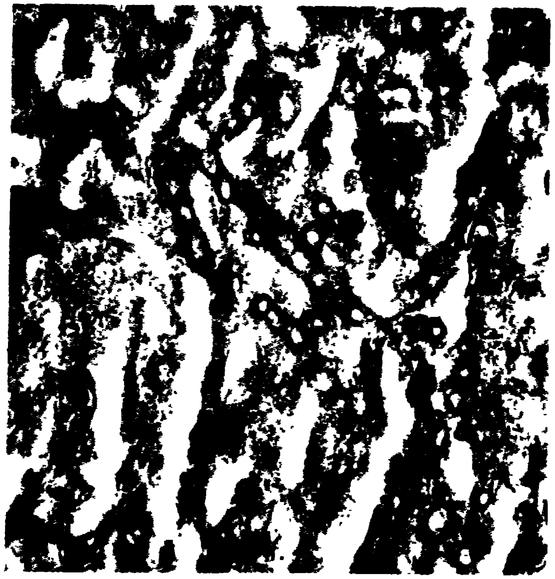

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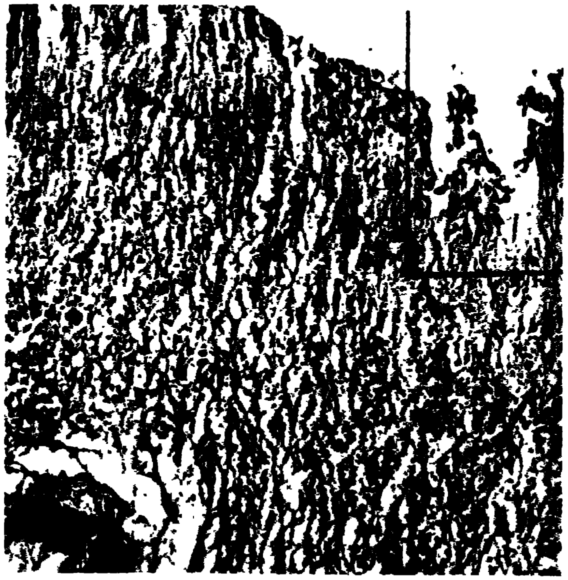

Fig. 4

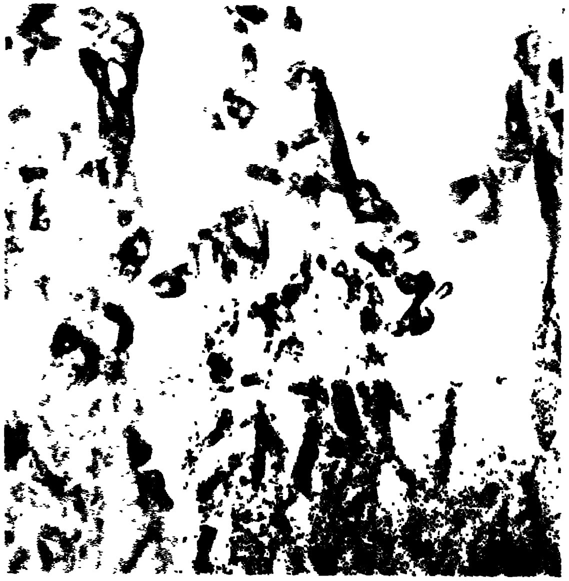

Fig. 5

Reddy et al.—Pulmonary and Gastric Aspergillosis (P. 384)

THE PROBLEM OF MALE INFERTILITY

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INTRODUCTION

A husband and wife faced with the problem of infertility are not bothered about the alarming rate of growth of population in various parts of the world. Theirs is a personal problem which needs sympathetic consideration and calls for intelligent investigation of possible defects in reproductive mechanisms. There is no doubt that investigation of infertility involves both husband and wife. Husband alone is thought to be responsible for infertility in about 30 per cent of cases. The author had the privilege to study the male partners of infertile couples being investigated in the sterility clinic of All India Institute of Medical Sciences, New Delhi, and thought it worthwhile to discuss the various problems encountered in infertile males.

The commonly accepted definition of infertility is that proposed by American Society for the Study of Sterility which states "A marriage is to be considered barren or infertile when pregnancy has not occurred after a year of coitus without contraception". The time period in this definition has been the subject of controversy and some writers extend it to two years.

AETIOLOGICAL FACTORS

Before we go to consideration of individual factors responsible for infertility in the male, it may be worthwhile to recapitulate the salient features involved in the male reproductive physiology. As we know, the testis is composed of two principal types of cells (i) seminiferous tubules which are concerned with spermatogenesis and (ii) Leydig cells which are concerned with androgen production. It seems logical to think that any abnormal state of the testis can result in infertility. The development and function of the testis is governed by pituitary and hypothalamus, so the cause of male infertility may lie primarily in the testis itself or this may be secondary to abnormal states of pituitary/hypothalamus.

(A) *Infections*—Infections like mumps, tuberculosis and syphilis occur frequently. Mumps orchitis occurs often enough for it to be considered as the possible cause in any case of male infertility. The incidence of mumps orchitis varies in different series from as low as 11 per cent to as high as 36 per cent (Velardo, 1958). If this happens before puberty, most will recover. In postpubertal affected males, atrophy of the testis occurs in about 50 per cent of cases. Bilateral orchitis occurs in 1/3rd of cases but bilateral atrophy is less common.

Syphilitic orchitis is an uncommon disease. Tuberculous involvement of the testis is usually secondary to tuberculous epididymitis.

Other bacterial infections may also cause involvement of testis but this is unusual.

(B) *Anomalies*—Cryptorchidism is the most important of maldevelopments that affect the testis. 0·1-0·3 per cent of testes are so affected (Velardo, *loc. cit.*). The undescended testis lacks the temperature regulation normally afforded by the scrotum and the higher intra-abdominal temperature results in testicular damage. Until early puberty there is no perceptible difference between retained testis and scrotal testis. After puberty this difference becomes progressively more evident.

(C) *Surgical procedures*—In herniorrhaphy, 1·52 per cent of patients (Baumrucker, 1946) had testicular atrophy. Operation for varicocele or hydrocele or any other procedure that needs handling of testis may be damaging.

(D) *Irradiation*—There is considerable individual variation in the dose of radiation required to produce sterility.

(E) *Testicular dysgenesis*—The most frequently encountered condition in this group is Klinefelter's syndrome. This disorder is characterised by gynaecomastia, aspermatogenesis, normal or increased Leydig cells and increased excretion of the follicle stimulating hormone. The testes are small, firm and histology is of sclerosing tubular degeneration with prominence of Leydig cells.

(H) *Maturation arrest*—Some patients presenting with infertility have normal male habitus, normal sized testes and normal levels of urinary gonadotrophins. The only abnormality is the arrest of maturation of spermatogenesis. The most commonly encountered point of arrest is at primary spermatocyte level. The underlying cause for this defect is not clear.

(G) *Germinal aplasia*—This is characterised by complete or almost complete absence of all cells of the germ cell line including the parent cells, the spermatogonia. This picture is seen after irradiation of testes and also in undescended testes of late adolescence.

(H) *Obstructive azoospermia*—It may be occassionally due to congenital defects. The commonest cause of acquired obstructive azoospermia is gonorrhoea. Tuberculosis is responsible less frequently and other infections prove rarely as aetiological factors.

(I) *Pituitary-hypothalamic disorders*—In about half of the cases of pituitary disorders, recognised lesions can be demonstrated by investigations; some of these patients may manifest as panhypopituitarism.

INVESTIGATION OF MALE INFERTILITY

(A) *History*—A thorough history taking is of crucial importance. The patient should be encouraged to give all relevant details. Details regarding sexual relations, frequency of coitus, orgasm, libido and premature ejaculations (if any) should be recorded. Past history of infections especially that of mumps, gonorrhoea, syphilis and tuberculosis should be enquired. History of trauma to the testes and that of surgical intervention round about testes should be specifically asked.

(B) *Clinical examination*—A detailed physical examination is essential. This should include measurement of body dimensions, muscular development, distribution and growth of pubic hair, pitch of voice and examination of male genital organs. The size and consistency of testes should be noted and epididymides should be palpated. One should be on the lookout for signs of hypopituitarism.

(C) *Laboratory investigations* — (a) Semen examination: This is the most important laboratory investigation in male infertility. The semen specimen should be obtained 96 hours or more after the last emission. It should be collected in a dry, clean, wide mouthed bottle by masturbation or if necessary by coitus interruptus. The patient must be instructed to collect the entire specimen of semen. The following seminal values are reported as compatible with fertility by the American Society for Study of Sterility:

(i) Liquefaction—usually complete with 10 to 30 minutes. (ii) Volume—2·5 to 5·0 ml. (iii) Motility (average findings at room temperature): After 2 hours—60 per cent to 70 per cent vigorous activity. After 6 to 8 hours—25 per cent to 40 per cent active, motile. (iv) Cell count (average normal)—60 million or more per ml. or a total of 150 to 200 or more mill. per ejaculate. Minimal normal standards—40 mill. per ml. with a total count of at least 125 mill. per ejaculate. (These values are not to be considered as absolute). (v) Morphology—Normal sperm heads should comprise 80 per cent or more of a total of at least 333 sperm heads counted.

It must be emphasised that when semen specimen proves defective, at least two more specimens should be examined at proper time intervals.

(b) Endocrine investigations: The employment of various endocrine tests should be guided by the clinical suspicion in a given case. Whenever there is suggestion of a secondary testicular involvement due to primary affection of the pituitary, complete pituitary function tests like x-ray skull, field of vision and perimetry, insulin sensitivity test, urinary gonadotrophin assays, adrenal functions and thyroid function tests (B.M.R., protein bound iodine and radio-iodine uptake) should be done.

(c) Chromatin sex: Certain infertile patients, may possess chromosomes and genetic traits quite different from the normal pattern and by means of special techniques, these chromosomal aberrations can be detected. For example, the presence of a chromatin positive pattern (female) in an overt male implies sterility. In such a situation there is no need for further physiologic or anatomic investigation for sterility.

(d) Other relevant laboratory investigations: Depending on a particular situation, other relevant investigations may be employed to find out the cause of infertility. For example, tests like blood and E.S.R., S.T.S., urine and x-ray chest may prove useful in the evaluation of systemic infections like tuberculosis, gonorrhoea and syphilis.

(D) *Testicular biopsy*—Testicular biopsy is a very important aid in the study of male sterility. It gives definite information as to the status of the testis. The testicular histopathology supplemented by semen examination provides answers in a large number of sterile males. The procedure is simple and harmless and should be advocated without reservations in the following situations:

(i) Cases with complete azoospermia on more than one examination. (ii) Cases with marked oligospermia not responding to simple therapeutic measures in 6 months' period. (iii) For evaluation of the effect of hormonal therapy in infertile males. (iv) For evaluating the status of cryptorchidism.

It may be helpful here to review the characteristic findings seen in testicular biopsies and to correlate the histopathological patterns with clinical situations.

(a) Normal testicular biopsy: Here the tubules are uniform in size. There is normal progression of spermatogenesis from large spermatogonia near the thin basement membrane through the mass of the tubule to the lumen, where mature sperms can be seen. This type of testicular biopsy can be found in: (i) men with normal semen, (ii) men with azoospermia but with some ductal (of vas) obstruction and (iii) infrequently in men with oligospermia.

(b) Complete aspermatogenesis: The tubules are uniform in size and shape but entirely devoid of any wheel and not compressed by the general cell. No therapy is indicated in such cases.

(c) Tubular sclerosis: Marked degree of tubular sclerosis is seen in cases of Klinefelter's syndrome. There is destruction and obliteration of tubules with marked thickening of the basement membrane. Tubular or peritubular sclerosis may be seen in some of the infective conditions of the testis.

(d) Spermatogenic arrest: The process of spermatogenesis is arrested at the stage of primary spermatocyte with the result that few or no sperms are seen. The arrested cells fragment and slough into the lumen of the tubules.

TREATMENT

It is the general experience that little change for good can be induced in most cases unless there is some recognisable cause for infertility. Hormonal therapy may prove useful in some cases, whereas surgical corrections may be desirable in some others.

(a) *Medical*—At the outset it is important to distinguish whether the sterility is due to primary defect in the testes or whether the testicular failure is secondary to lesions in the pituitary or hypothalamus. In secondary testicular failure chorionic gonadotrophin is likely to be beneficial. It is usual to start these patients on a dose of 1000 i.u. of gonadotrophins twice a week and note the response within 6-12 weeks.

In primary testicular failure, the result of hormone therapy depends upon the basic pathological lesion. Earlier cases of spermatogenic arrest can sometimes be beneficially treated with androgens. The patients with complete primary testicular aspermatogenesis and Klinefelter's syndrome will rarely respond to androgen therapy. Another aspect of medical treatment of infertility in male which may be of value lies in the possibility of improving the ejaculatory performance for a few days at a time by administration of testosterone, 5-10 mg. daily for 10-12 days, starting cycle day 3 to 5 and repeated over several cycles.

The brief interludes of androgenic treatment do not permanently damage spermatogenesis.

(b) *Surgical*—It seems logical to think that correction of obstruction in cases of obstructive azoospermia should prove helpful. Obstructions in epididymis can be overcome by epididymovasostomy if the vas is patent. The procedure is beneficial in about 80 per cent of cases of inflammatory strictures if tuberculous cases can be excluded. The success rate in congenital obstruction, however, is only 10 per cent (White and Green-Armytage, 1962). Nothing can be achieved in cases of infertility associated with bilateral cryptorchidism.

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SPECIAL ARTICLES

TREATMENT OF A CASE OF CANCER WITH M-XYLOHYDROQUINONE

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In his last years Professor J. B. S. Haldane suffered from cancer of the rectum and was admitted in the London University College Hospital. The growth was removed and colostomy was done. During operation it was noted that there were extensive metastases, particularly in the liver; although this was not communicated to the patient.

In March 1964, he returned to India. His body weight had come down to 80 Kg. By September 1964, his weight was reduced further to 70 Kg. and he became prostrated. The liver had gone down to the iliac crest and was hard and nodular and caused much pain. There was accumulation of large amount of fluid in the abdomen and there was marked oedema in the lower limbs. Anaemia was evident and there was constant hiccup. There was constant nausea and the daily intake of food was very little and consisted of only one glass of milk, one egg and a few teaspoonfuls of *ukma*, some rice and a little vegetables and sweets. The only thing he seemed to like was plenty of cold water. He had no relief even with tr. opii, codeine phos. and aspirin.

At this stage of illness and in this condition, he took a great deal of interest regarding the probable efficacy of m-xylohydroquinone in the treatment of cancer. He discussed with the author the results of the ani-mitotic effect of this compound on the root tip cells of *Allium cepa*. In the third week of September, 1964 he volunteered for treatment with m-xylohydroquinone. Injection of solution of m-xylohydroquinone, 2·5 ml. (10 mg./ml.) on alternate days was started along with oral administration, both in liquid form and pills.

Daily about 900 mg. was administered orally and 25 mg. by parenteral route on alternate days. After ten days, the injections were given once every fourth day, till the end of November, 1964. Opiates, vitamin B complex, digestive pills, esidrex, etc., which he had been taking so long, were continued. He procured the photograph of the portion of the rectum with the cancerous growth (Fig. 1) kept in the London University College Hospital and also the microsections of the tumour and handed them over to the author. Eventually, Prof. Haldane breathed his last on the 1st day of December 1964, at the age of seventy-two.

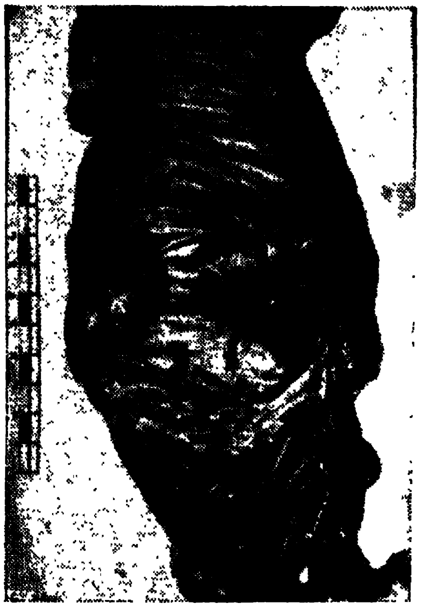

FIG. 1 SHOWING PORTION OF THE RECTUM WITH THE CANCEROUS GROWTH

CHANGES OBSERVED

Although the new treatment was begun at a very advanced state of the disease, some gross changes were observable in the overall general reactions. It was reported after a week that the movement of the patient was apparently more free and brisk. After the first day's administration, the hiccup was greatly reduced. After two days of administration of the drug, the liver pain considerably abated. When examined after a fortnight, it was noted that the liver had receded slightly but the oedema of the legs was still there. After a month it was reported that the patient had lost another 1·5 Kg., i.e. his weight had gone down to 68·5 Kg. On examination, it was noted that the swelling of the legs was almost gone and the fluid in the abdomen was appreciably reduced. It was evident that the patient had lost at least 3 Kg. of accumulated fluid. The liver was noted to be six fingers below the costal margin. Again during the post-mortem examination it was reported to be only four fingers below the costal margin.

After the first day's administration of the drug, his urine became dark green in colour and there was apprehension that this might be due to the toxic effect of the drug or due to the elimination of melanin-like substances. This apprehension was removed when it was known that the patient was being given vitamin B complex injections and the colour observed was due to oxidised m-xylohydroquinone which was being eliminated in the urine. It is well known that all anti-mitotic drugs are usually toxic and cannot be administered continuously for an indefinite period. In the case of m-xylohydroquinone it was different, and this drug had previously been administered to numerous patients as an oral contraceptive, and also to more than 500 patients for metropathia haemorrhagica. However, after two months of treatment, blood count and other biochemical examinations of the blood were done, the reports of which are given below.

INVESTIGATION REPORTS

BLOOD COUNT :

	8-7-64	28-7-64	26-11-64* (After the accident)
Hb. ...	13 g.%	12 g.%	8·70 g.%
R.B.C ...	3,440,000	3,420,000	3,210,000
W.B.C. ...	9400	12,200	13,125
Poly. ...	85%	74%	95·5%
Lympho. ...	12%	21%	7·0%
Eosino. ...	3%	5%	2·0%
Mono. ...	0%	0%	5·0%
Baso. ...	0%	0%	0·5%

*Toxic neutrophils, anisocytosis, hypochromic red cells present.

URINE EXAMINATION (21-9-64) :

Sp. Gr.—1007. Albumin—Distinct trace. Casts—None found. Pus cells—Few. No other abnormalities detected.

BIOCHEMICAL EXAMINATIONS OF BLOOD :

7-11-64
Fasting blood sugar ... 100 mg.%
26-11-64
Urea ... ... 37 mg. per 100 ml.
N.P.N. ... ... 40 mg. per 100 ml.
Alkaline phosphatase ... 10 K.A. units.
Thymol turbidity test ... 6·5 units.
Total protein ... 4·6%
Albumin ... ... 2·5%
Globulin ... ... 2·1%

BODY WEIGHT RECORDS :

16-10-64	... ...	70·5 Kg.
23-10-64	... ...	70·0 Kg.
30-10-64	... ...	68·5 Kg.
6-11-64	... ...	70·0 Kg.
13-11-64	... ...	72·0 Kg.
20-11-64	... ...	70·5 Kg.*

*After the accident and with empty colostomy bag.

From the comparative studies of the blood count reports it is evident that from 8-7-64 till 28-7-64 the loss of haemoglobin was 1 g. in twenty days and the red cells were also reduced from 3·44 million to 3·42 million. Although no such blood count was done at the beginning of the present trial yet after about two months haemoglobin was still 8·7 g. and the red cells were 3·21 million. Biochemical reports suggest that 50 per cent of the liver was still working.

ACCIDENTAL SETBACKS

After one month's treatment with this compound, Professor Haldane was accidentally bitten by a cat. The local physician started penicillin immediately and after a day or two cerebral symptoms developed. Fortunately, when penicillin was discontinued, the symptoms subsided. Again within a month, the Late Professor accidentally fell down when he received a heavy blow on the head and his right side. Bleeding was profuse and pain developed on the lower part of the right side of the chest and the right knee also became swollen. This was serious, as there was extensive metastasis in the liver, etc. The patient died 17 days after the incident.

POSTMORTEM REPORT

It is not possible to include a detailed report of postmortem examination within the small compass of this article. Only the relevant portions will be mentioned. Weight of the liver was 5·64 Kg. Nodules of varying size and shape were seen. Most of the left lobe of the liver was intact whereas the right lobe was completely replaced by secondary deposits. There were umbilications, extensive areas of necrosis and infection. There were two cysts also. On cut sections, some of the big nodules showed evidence of necrosis. Microscopical sections of the liver showed replacement by adenocarcinomatous tissue in several areas. There were evidence of infection and also necrosis in the nodules. Two lymph nodes in the porta hepatis were enlarged but did not appear to produce any pressure on the structures at porta hepatis. The surface of the pancreas was studded with nodules. There were two small secondary deposits on the outer side of the right kidney and also a small nodule on the cut surface. There was one small secondary nodule at the lower pole of the kidney. Both the kidneys showed evidence of senile sclerosis and pyelonephritis. Right suprarenal gland showed diffuse infiltration with malignant cells and haemorrhage and the left one showed a well circumscribed metastatic nodule almost replacing the entire gland. Diaphragm, hilar lymph nodes, lymph nodes in the deep cervical region and also at porta hepatis, etc., showed evidence of partial replacement by adenocarcinomatous tissue with extensive areas of degeneration. There was also an adenoma in the thyroid. The anatomical diagnosis was secondary adenocarcinomatous deposits in the liver, kidney, suprarenals and lymph nodes with extensive atheromatous changes in the blood vessels, and mild chronic pyelonephritis of kidneys and adenomatous nodule of the thyroid. Cause of death was malignant cachexia due to extensive secondary deposits from an adenocarcinoma. The pathologist gave his opinion in the following lines: "In general, I found that the cancerous tissues found in the liver, kidneys, suprarenals, etc., were showing marked tendency for necrosis and also I feel, that the malignant cells were not showing much mitotic activity".

Subsequently when both sets of slides, i.e., the London slides of sections of the primary tumour (Figs. 2, 3 and 4, *vide* Plate, showing adenocarcinomatous growth beneath the villi, × 50, lymph node of the intestine, × 50, and lymph node of the intestine, × 80, respectively) and the Kakinada slides of sections from secondary growths, removed after treatment with m-xylohydroquinone (Figs. 5, 6 and 7, *vide* Plate, showing necrosed metastatic adenocarcinomatous nodule in the liver, × 80, discrete adenocarcinomatous infiltration in the glomeruli of the kidney, × 50, and partially degenerated metastatic nodules in the suprarenal, × 50, respectively) were examined and their cell counts were done, the above opinion became evident. In the London slides, as much as 0·81 per cent of the cells were found in a state of mitosis whereas in the Kakinada slides only 0·33 per cent of the cancer cells showed mitotic activity.

	Total cells counted	Mitotic cells	Amitotic cells
London slides ...	603	5	598
Kakinada slides ...	1667	5	1662

N.B.—In the chi-square test $\lambda^2 = 2{\cdot}8$ and the degree of freedom = 1.

It is slightly significant at 10 per cent level. But from the fact that m-xylohydroquinone brings about an arrest at metaphase, the total of 5 cells found in the state of mitosis in the Kakinada slide is in fact a sum total of several metaphases (which must have taken place previously), it may be surmised that the change may be statistically significant, i.e., this change in the rate of mitosis is not per chance but due to the effect of an agent administered for the purpose.

DISCUSSION

Treatment with m-xylohydroquinone was started at the last stage of the disease and treatment could be continued for nine weeks only. The only result reflected was in the amelioration of pain in the liver, the lower margin of which also receded from the iliac crest to about four fingers below the costal margin. The accumulated fluid in the lower limbs was almost gone and the fluid in the abdomen lessened. The weight of the patient increased from 68·5 Kg. to 72 Kg. From the above results it may be concluded that this compound might be effective, at least to some extent, in arresting the progress of the metastatic growths. This has further been corroborated from the comparative studies of the two groups of slides namely, London slides (before treatment) and the Kakinada slides (after treatment). It was observed that there was degeneration and necrosis in the metastatic nodules in the Kakinada slides and also the rate of mitosis as compared to that in the London slides was much reduced. Question may be raised that normally umbilication is encountered in the liver, but here in this case there was found usual umbilication as well as degenerated metasstatic growths, as mentioned in the postmortem report. In the necrosed cancer nodule, the central portion was found degenerated while the adenocarcinomatous cells, lining the nodule, still persisted. Compared to other antimitotic drugs, like nitrogen mustard, alkylating agents, etc., its toxicity range is very wide and may safely be administered continuously and for a prolonged period. In fact, one case of squamous cell carcinoma of the vagina is being treated with this compound for the last two years with some positive improvement. A few more cases have also been treated subsequently with this compound with encouraging results.

The antimitotic effect of this compound, m-xylohydroquinone, was previously observed in the root tip cells of *Allium cepa* and arrest at metaphase was observed. It was further learnt from the literature that quinones, hydroquinones and phenols have antimitotic effects similar to those of ionic radiation. Further spectrophotometric studies, conducted in this laboratory, suggest that m-xylohydroquinone interacts with D.N.A. Pure D. N. A. has an absorption maxima at 260 mμ but when interacted with m-xylohydroquinone, the absorption density at the same region, 260 mμ is enhanced sufficiently. Also the calculated and observed curves intersect each other. The absorption maxima of m-xylohydroquinone is at 290 mμ. From the above considerations it may reasonably be supposed that m-xylohydroquinone may be effective at least in arresting the growth of cancer, and may be helpful in the prolongation of life with some relief of symptoms.

ACKNOWLEDGMENT

The author gratefully acknowledges the services rendered by Dr. P. Ramachandra Rao, Professor of Pathology, Rangaraya Medical College, Kakinada, Andhra Pradesh, by sending him the postmortem reports and the microsections of the isolated metastatic nodules of the various viscera of Late Prof. J. B. S. Haldane. He is thankful to Dr. Sushanta Sarkar, Assistant Professor of Pathology, N. R. S. Medical College, Calcutta, for doing the cell counts from the slides, and to Dr. C. R. Das Gupta, retired Professor of Haematology, School of Tropical Medicine, Calcutta, for doing the last blood examination of the patient. The author is specially grateful to Mrs. Helen Spurway Haldane and to the devoted assistants of the late Professor, for supplying him with many valuable reports.

ATAXIA

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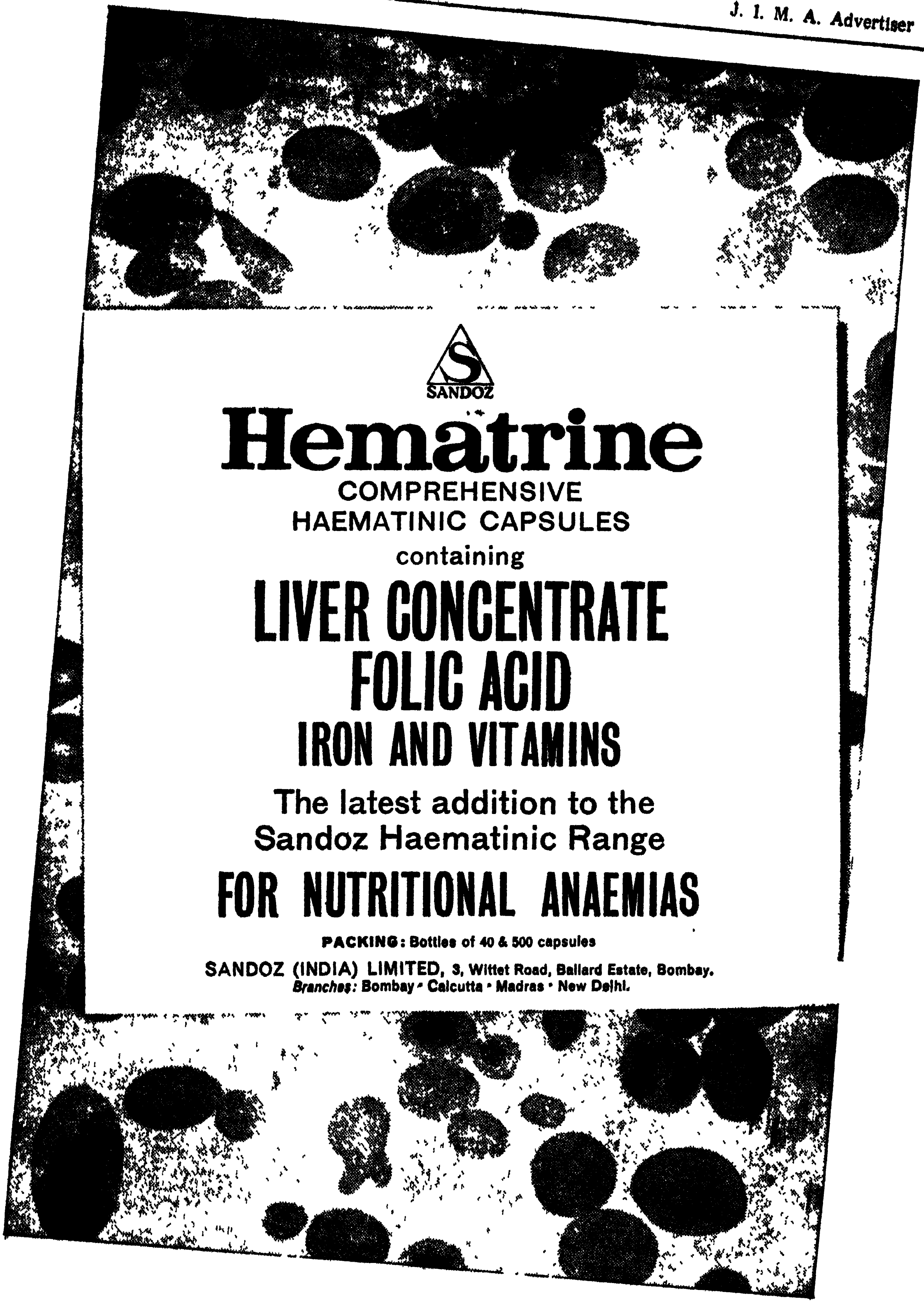
Ataxia, by definition, is a disorder of voluntary movement with incoordination. The two main types are cerebellar and sensory or spinocerebral ataxia. Other rarer types which are to be considered subtypes are also described.

CEREBELLAR ATAXIA

It is caused by lesions affecting the cerebellum and/or its connections, afferent as well as efferent. The range and power of movement, are inappropriate to the needs of the movement, with consequent incoordination, dys-synergy and 'decomposition of movement'. Overshooting the mark is a frequent result. Clinically, this ataxia is demonstrable by the well-known heel-knee and finger-nose tests. Unilateral cerebellar lesions cause ataxia of the limbs on the same side as the lesion, a tendency to veer to side on walking, with the affected lower limb overstepping and overabducting, and a marked difficulty in negotiating corners or in turning around. The trunk is bent



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with the concavity towards the involved side, the affected shoulder is carried slightly in advance and the head is slightly deviated to the same side. The patient often falls, to the same side. Other signs of cerebellar disease such as nystagmus, coarse swaying tremor, hypotonia, rebound phenomenon, pendular knee jerks and difficulty in performance of rapid repetitive movements, may be present. The tendon reflexes are often depressed due to hypotonia. Dysmetria and hypotonia also contribute to the ataxic deficit and towards the inability to do repetitive movements rapidly (dysdiadochokinesis). The gait of a cerebellar ataxic is wide based and he uses his arms for balance, very much like the circus acrobat on the tight rope.

With midline cerebellar lesions, the gait is typically swaying and staggering. There is gross disability in maintenance of posture. The patient falls frequently and in no particular direction. Signs of lateralisation and nystagmus are usually absent. Bilateral lesions produce a drunken type of gait and bilateral signs.

CASE REPORT

Case 1—H., a male aged 24, was seen with a history of fever, headache, vomiting and inability to walk due to unsteadiness, for one week. Mental functions were normal. The cranial nerves were all normal apart from nystagmus to the right side. There was no paresis or sensory deficit. Muscle tone was depressed on the right side, which had ataxia in the limbs. The reflexes were normal except for a tendency to pendular type of knee jerk on the right. Rebound phenomenon and dysdiadochokinesis were elicited on the right. Romberg's sign was negative. The C.S.F. contained 12 white cells per c.mm., majority of them being lymphocytes. His V.D.R.L. reaction was negative. The x-rays of the skull were normal. He was treated as a case of acute cerebellar syndrome, probably encephalitic. Broad spectrum antibiotics were given and he made a complete recovery. Disseminated sclerosis, remained a possibility here.

The site of the lesion in cerebellar ataxia may be in the spinal cord or brain stem, involving the relevant tracts. They may be of vascular, neoplastic, inflammatory, demyelinating or degenerative nature. Intoxications as with phenytoin, can result in a cerebellar syndrome.

SENSORY ATAXIA

In sensory ataxia the picture is quite different. The ataxia is always worse in the dark or when the patient closes his eyes. It is common experience to see patients who give a history of feeling unsteady when they wash their face, or when they pull articles of clothing over their head while dressing, occasions when their eyes are likely to be closed. The patient walks and stands on a wide base. The most characteristic feature of the gait however, is the attempt made to compensate for the loss of proprioceptive sensations (joint and position sense), which normally provide information regarding the position of the limbs and their parts in space, by relying on the visual apparatus. The patient, therefore, has his eyes glued to the floor while he walks. The gait is also high-stepping. Romberg's sign is positive, again showing the dependence on visual pathways. There are no cerebellar signs. On objective testing, deficits in joint and position sense are demonstrable. The state of the tendon reflexes and muscle tone, depends on the level of the lesion and the integrity of the pyramidal tracts.

Lesions in the peripheral nerves, the posterior columns or the higher sensory areas, cause a loss of gnostic sensation. Appreciation of postition and joint sense, are vital in the proper performance of all voluntary movements, but can to a certain extent be compensated for, by visual impulses, which provide an alternate route for the recognition of the position of limbs, nature of the terrain and other valuable information. Hence the ataxia becomes more marked when the eyes are closed or when it is dark.

CASE REPORT

Case 2—K., a male aged 34, with a past history of incompletely treated syphilis, had been unsteady on his feet for 2 years, during which he had paraesthesia in the limbs and difficulty in the act of micturition. On examination, the pupillary reactions were suggestive of an Argyll Robertson type. He had mild bilateral ptosis with compensatory overaction of occipitofrontalis, hypotonic lower limbs, absent joint and vibration sense appreciation, abnormally brisk knee jerks, absent ankle jerks, extensor plantar responses and a gait highly characteristic of sensory ataxia. The upper limbs were normal. Romberg's sign was present. The blood V.D.R.L. test was positive in a significant dilution and the C.S.F. protein content was elevated, at 65 mg. per cent. A diagnosis of taboparesis was made. He made a partial recovery with a course of penicillin and is attending for regular follow-up.

COMBINED SENSORY AND CEREBELLAR ATAXIA

Sensory and cerebellar ataxia, may be present together in the same patient. Such a state can occur in disseminated sclerosis, in the case of anomalies of the foramen magnum region and in the group of hereditary ataxias that includes Friedreich's ataxia. In Friedreich's ataxia which is a heredofamilial disorder, a degenerative process affects the pyramidal and spinocerebellar tracts in the latreal column and the sensory tracts of the posterior columns conveying proprioceptive forms of sensation. The disease manifests in early life, usually between the 5th and 15th years.

CASE REPORT

Case 3—H., a male aged 28, with gradually increasing weakness of both legs, unsteadiness of gait since the age of 12, difficulty in articulation for the last 8 years and involuntary flexor spasms in both legs for 5 years, had no similar major disability in the family history. Mental functions were normal. His speech was explosive in character. Nystagmus was noted in both vertical and horizontal planes. There was a spastic paresis of all four limbs, with a marked diplegic element in the legs. He had a scissors' type of gait and could take only about a dozen steps before falling, due to severe ataxia. Incoordination, dysdiadochokinesis, rebound phenomenon and pendular knee jerks could be easily demonstrated. All tendon reflexes were markedly exaggerated except for the ankle jerks which were absent. Patellar clonus was seen bilaterally and the plantar responses were of the extensor type. The abdominal reflexes were absent. Vibration sense was lost in the legs and joint sense markedly impaired in the toes. Pes cavus deformity and moderate scoliosis were the other abnormal findings. A brother, who was the only relative available for examination, had bilateral pes cavus, and no other abnormal central nervous system signs. A diagnosis of hereditary ataxia of the Friedreich's type was made. X-ray studies of the skull and spine did not show any unexpected findings. He was managed on symptomatic lines.

OTHER TYPES OF ATAXIA

Involvement of the vestibulo-cerebellar pathways often produce a combination of vertigo and ataxia. As the ataxia is of the cerebellar type, this group is not considered a seperate entity.

The role of the frontal lobe in the causation of ataxia, has in recent years aroused great interest. Ataxia is seen in frontal lobe tumours, only as a late manifestation, when generalised rise of intracranial tension, produced cerebellar displacement. Meyer and Barron (1960) in their classic paper on frontal lobe apraxias considered that ataxia can occur with lesions on the medical aspect of the frontal lobes, ameterior to the motor cortex. Here, the ataxia however, is contralateral and is probably due to interruption of the fronto-ponto-cerebellar circuit. Hence this type of ataxia, is in the final analysis, again cerebellar. Scanning speech, dysmetria and dysdiadochokinesis are absent in ataxias of frontal origin. Bizarre disturbances of movement are sometimes present. Steps tend to be short and shuffling and feet move as if they are glued to the floor, in walking. Retropulsion may be seen. The patients often have

TABLE 1—SHOWING DETAILS OF CASES FROM CALICUT AND A TEACHING HOSPITAL IN LONDON

No.	Name	Age (years)	Type	Diagnosis	Duration	Progress
				(A) CALICUT SERIES		
1	K.	45	Cerebellar	Brain stem ischaemia	2 weeks	No response
2	C.	68	do	do	4 weeks	Partial recovery
3	H.	24	do	?Encephalitis ?Disseminated sclerosis	1 week	Recovered
4	M.	50	do	Acoustic neuroma	2 years	Refused surgery
5	P.	35	do	Cerebellar abscess	1 month	Recovered
6	A.	33	do	Primary cerebellar degeneration	4 years	No recovery
7	M.	45	Sensory	Spondylolisthesis	6 months	Recovered
8	C.	45	do	Post-gastrectomy vitamin B_{12} neuropathy	9 months	Partial recovery
9	G. N.	45	do	Vitamin B_{12} neuropathy	3 months	Recovered
10	U.	55	do	Peripheral neuritis	1 year	Partial response
11	R.	80	do	Peripheral neuritis ?Beri-beri	3 months	Recovered
12	S. K.	56	do	Diabetic neuropathy	2 years	No response
13	A.	63	do	do	2 months	Partial response
14	K.	30	do	Hansen's disease	1 year	Transferred
15	K.	34	do	Taboparesis	2 years	Partial recovery
16	A. D.	62	do	Ischaemic myelopathy	2 months	No response
17	V.	59	do	Tabes dorsalis	2 years	Partial response
18	A.	30	Mixed	?Disseminated sclerosis	2 weeks	Recovered
19	H	28	do	Friedreich's ataxia	16 years	No response
20	R.	55	do	Meningovascular syphilis	1½ years	No response
21	N. N.	65	do	Cervical spondylosis and basilar ischaemia	2 years	Partial response

TABLE 1—(*Contd.*)

No.	Name	Age (years)	Type	Diagnosis	Duration	Progress
				(B) LONDON SERIES.		
1	S. A.	24	Cerebellar	?Disseminated sclerosis	2 days	Recovered
2	L. A.	54	do	do	1½ years	No recovery
3	C. B.	35	do	do	6 years	do
4	I. V.	40	do	do	5 years	do
5	I. T.	36	do	do	2 years	do
6	J. P.	48	do	do	17 years	do
7	R. S.	38	do	do	3 months	Recovered
8	J. C.	22	do	do	1 year	Partial recovery
9	F. C.	58	do	do	8 years	No recovery
10	G. P.	40	do	do	4½ years	do
11	G. M.	39	do	do	1 year	do
12	J. K.	66	do	Acoustic neuroma	9 months	Refused surgery
13	E. P.	72	do	do	1 year	Recovered
14	W. H.	66	do	Cerebellar abscess	1½ years	Partial recovery
15	G. S.	63	do	Primary cerebellar degeneration	1 year	do
16	T. B.	62	do	Cerebellar vascular disease	5 years	do
17	S. S.	59	do	Brain-stem infarction	4 years	do
18	G. E.	27	do	Phenytoin intoxication	3 days	Recovered
19	A. H.	44	do	do	6 weeks	do
20	F. P.	52	do	Undiagnosed	2 years	do
21	V. W.	46	? ?	Hysterical	7 years	do
22	W. L.	39	Sensory	Vitamin B_{12} neuropathy	4 months	Recovered
23	E. M.	77	do	Ischaemic myelopathy	5 years	No recovery
24	C. C.	67	do	Polyneuritis	7 years	Died
25	C. W.	39	do	do	3 years	No recovery
26	N. R.	69	do	Tabes dorsalis	20 years	do
27	W. R.	66	do	Neurosyphilis	15 years	do
28	G. A.	64	do	Tabes dorsalis and spondylolisthesis	6 months	Partial recovery
29	M. D.	68	do	Taboparesis	18 years	No recovery
30	S. T.	46	do	Meningovascular syphilis	6 years	do
31	E. A.	66	do	do	8 years	do
32	K. W.	72	do	Undiagnosed	10 years	do
33	A. R.	50	Mixed	Hereditary ataxia	14 years	do
34	E. G.	20	do	do	12 years	do

difficulty in getting up from the sitting position. Clearly, the role of the frontal lobes, if any, needs further clarification.

STUDY OF A SERIES OF CASES FROM CALICUT AND A TEACHING HOSPITAL IN LONDON

At a general medical unit of the Medical College Hospital, Calicut, during a period of 14 months ending May, 1964, 21 patients who were primarily problems in ataxia, were personally observed, as in-patients. These formed 16 per cent of all primarily neurological patients admitted into the unit. 11 had sensory ataxia, 6 cerebellar ataxia and 4 had mixed type of ataxia.

Comparison with a small personal series, collected at the neurology unit of a teaching hospital in London, by the author, is revealing. 34 cases comprise this series as follows. The relevant details are shown in Table 1.

DISCUSSION

The average age of the Calicut series was 48, that for the cases of cerebellar ataxia being 42·5 and the average for the sensory ataxia cases being 52. The corresponding figures for the cases seen at London was 51 years for the whole series, 47·3 for the cerbellar cases and 61 for the sensory ataxias. If all cases of disseminated sclerosis which admittedly is a rare disease in India but accounts for 11 out of 34 cases in the London series is excluded, the average for the whole group in this series stands at 56·5 and for the cerebellar cases at 56·8. If the sole case of suspected disseminated sclerosis is excluded, the average age of the cases of cerebellar ataxia, seen at Calicut moves to 46. The difference in the average age is completely in keeping with the higher average of the general population in Britain.

When the aetiological factors are considered, the most striking feature as expected, is the high incidence of disseminated sclerosis among the British group. There are 11 cases, with an average age of 39·5. All these cases had cerebellar ataxia, thereby causing a preponderance of this type of ataxia in the group. It might be thought that this being a specialised neurological unit, could have caused this high percentage of disseminated sclerosis. But experience at two other centres in the U.K., one general medical and the other neurological, only served to confirm the impression that disseminated sclerosis accounts for a large proportion of cases of ataxia.

In fact, the incidence of disseminated sclerosis, is not fully revealed by these figures, as many cases seen during this period, were very advanced cases, most of them bed or chair-ridden patients who were not primarily problems in ataxia and were excluded. It cannot be denied that this disease does exist in India. In the U.K. however, it is almost a major national problem, that places a terrific strain on hospitals, clinics, physiotherapy departments, rehabilitation units and social workers.

Phenytoin intoxication, is not yet a common entity in India, where only a minute percentage of epileptics are on regular medication with anticonvulsant drugs.

•Neurosyphilis, accounted for under 10 per cent of the Calicut cases and nearly 18 per cent of the London ones. The number of cases is too small to warrant any statistical conclusions. The same applies to vascular disease which makes up 18 per cent of the Indian cases and only 9 per cent in the British group. This is especially so as the majority of the elderly disabled people in the U.K., are to be seen in geriatrics wards and old peoples' homes, and they are patients more likely to have vascular disease of the nervous system. Ataxic children are not included, as at both centres, they were seen by the paediatricians.

There can hardly be any comparison between the investigative and therapeutic facilities available at London and at Calicut. But in only 3 of the cases at Calicut the diagnosis was in doubt. In 2 out of the 34 cases at London, the diagnosis could not be established. It is only rarely that highly specialised techniques are needed to establish the diagnosis in these cases. There are no substitutes for a well taken history, a careful neurological examination and a methodical approach.

From the therapeutic angle, on the other hand, the lack of facilities specially of tranied physiotherapists was badly felt. 6 out of 21 made a complete recovery and 7 improved partially. In the British series, 6 out of 34 recovered fully and 2 partially. This does not justify any tall claims, as the aetiological factors and duration of the symptoms had a great deal to do with the prognosis. The average duration in the Calicut series was under 2 years, and in the British cases 5½ years. The average for the cases that did not recover in the latter series was as high as 7½ years. Again 8 of the 11 cases of desseminated sclerosis had a long history and stable deficits which could not be expected to improve.

SUMMARY

The various types of ataxia and their neurological basis are described. A small series of 21 cases seen at Calicut, is presented. This is compared in general terms with 32 cases seen personally at a centre in the U.K.

The most striking feature is the high incidence of disseminated sclerosis in the latter group. This preponderance and its influence on the average age, prognosis and the proportion of the two main types of ataxia is commented on.

ACKNOWLEDGMENTS

I am grateful to Dr. C. A. Pallis, Consultant Neurologist at the Hammersmith Hospital, London, for stimulating my interest in the subject and for permission to use materials collected at his unit. I am thankful to Dr. Vincent D. Bayliss, Professor of Medicine, Medical College, Calicut, for encouragement, and to Dr. M. Thankam, Superintendent, Medical College Hospital and Dr. R. Anantanarayanan, Principal, Medical College, Calicut, for permission to publish this paper.

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DIGITALIS TOXICITY*

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William Withering introduced digitalis in modern medicine in 1775 after ten years of intensive study. Very little progress has been achieved since his classical description of the drug. At the same time he warned that care should be taken while administering the drug or otherwise "the medicine, of so much efficacy, will be condemned and rejected as dangerous and unmanageable."

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* Paper read at Mysore State Medical Conference, Hubli, October, 1964.

Being a cumulative drug with low therapeutic index, digitalis is bound to show toxicity in one way or another. In recent years there seems to be an increase in the incidence of digitalis toxicity. It is due not only to the increased awareness of the condition but also to increased use of diuretics and corticosteroids with attendant hypokalaemia, and other measures in the management of congestive heart failure. The lowered cellular potassium and hypercalcaemia favour toxicity.

SIGNS AND SYMPTOMS

Very little has been added to the original description of Withering: "Foxglove when given in very large and quickly repeated doses occasions sickness, vomiting, purging, dizziness, confused vision, objects appearing green or yellow, slow pulse, cold sweats, convulsions, syncope, and death". The only manifestation he has not mentioned is about the various cardiac arrhythmias.

Gastro-intestinal—Anorexia, nausea, vomiting and diarrhoea. These symptoms may not be the presenting ones as popularly believed.

Visual—Yellow or green vision, and scotomas.

Neurological—Fatigue, insomnia, depression, headache, vertigo, and convulsions.

The visual and the neurological manifestations are less common. Gynaecomastia and rarely allergic manifestations have also been observed.

Cardiovascular—These are the most important manifestations as they are serious and may be the presenting symptoms.

Bradycardia—This is sinus in type and the heart rate is one of the guiding principles in digitalis therapy.

Premature systole—The premature systoles are more often ventricular and multifocal. The presence of coupled rhythm is very characteristic.

Case 1—The patient, aged 50 years, had chronic bronchitis with cor pulmonale. He had digitalis leaf, gr. 2, t.d.s. with diuretics for a period of one month. He developed coupling and returned to normal when the drug was withdrawn (Figs. 1 and 2). It is interesting to note that the serum potassium level was 5·17 mEq./l.

Tachycardias—The common type is supraventricular tachycardia with or without block, followed by ventricular tachycardia and bi-directional tachycardia. When there is supraventricular tachycardia with block the pulse rate may be more than normal giving a false impression that the digitalis may be insufficient. Ventricular tachycardia is a dangerous rhythm change and may lead to ventricular fibrillation and death. Bi-directional tachycardia is a very rare type of arrhythmia. Of the 35 examples quoted so far, 28 are due to digitalis and only 25 per cent of cases

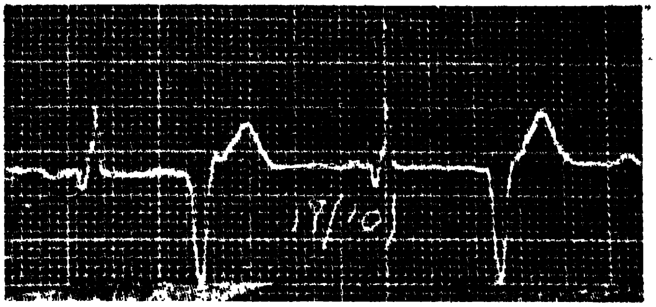

FIG. 1—SHOWING COUPLED RHYTHM

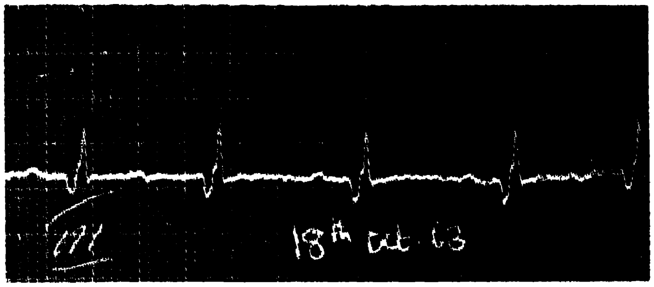

FIG. 2—SHOWING NORMAL RHYTHM AFTER WITHDRAWAL OF THE DRUG

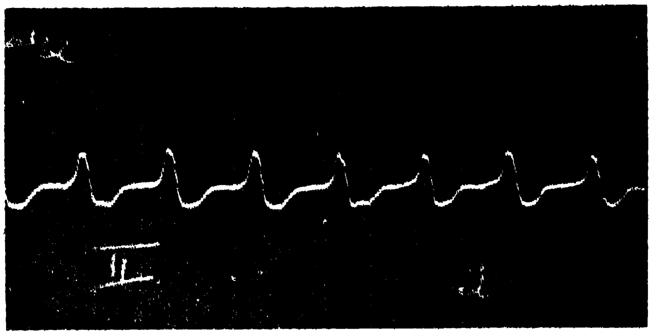

FIG. 3—SHOWING VENTRICULAR TACHYCARDIA

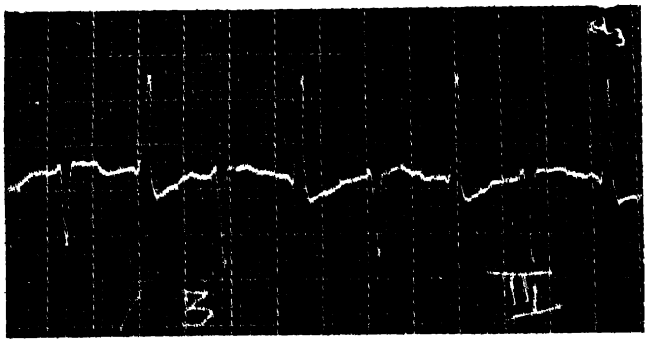

FIG. 4—SHOWING BI-DIRECTIONAL TACHYCARDIA

survived. Digitalis has failed to produce this arrhythmia in a healthy heart.

Case 2—The patient, aged 70 years, was on digitalis and diuretic therapy for two months, and was admitted for having marked tachycardia. She was diagnosed to have congestive heart failure due to arteriosclerotic heart disease. The E.C.G. showed nodal tachycardia with a heart rate of 170 per minute, followed by ventricular tachycardia, bi-directional tachycardia, and again nodal tachycardia (Figs. 3, 4 and 5). It is important to note the varying rhythms in such a short time.

Different degrees of heart block—S.A. block, I, II, III degrees of heart block.

Case 3—The patient, a girl aged 3 years, was admitted with a history of swallowing 30 tablets of digoxin. She vomited after 3 hours. Twenty-four hours' check-up with E.C.G. was maintained and the following tracings showed sinoatrial block, prolongation of P-R interval, 2 :1 block and 4 :1 block (Figs. 6, 7 and 8). The patient was treated with 3 g. of potassium intravenously over a period of 24 hours. This case illustrates the action of digitalis on a physiological heart. The vomiting which occurred after 3 hours suggests the action to be central.

Atrial fibrillation and bundle branch block are rare features of digitalis toxicity. The S.T. depression and T inversion as seen in E.C.G. tracings only suggest digitalis effect and not the toxicity.

RECOGNITION OF DIGITALIS TOXICITY

This is mainly based on high index of suspicion and awareness of the condition as in all toxicity problems. The association of digitalis administration, signs and symptoms of toxicity and recovery after withdrawal of the drug is easy to think about retrospectively, but when one is faced with the problem at the bedside it may be difficult to decide. Even at postmortem no specific changes are seen.

The gastro-intestinal symptoms may not be the presenting symptoms and may be the manifestation of the disease itself. Nowadays it is common to find cardiac arrhythmias as the presenting feature, and even then they may be transient and varying as seen in Case 2. Again these rhythm changes may be manifestations of the disease itself.

Case 4—A patient aged 59 years was diagnosed as having myocardial infarction with failure. He was on digitalis leaf, gr. 2, t.d.s. for one week, and gr. 1, t.d.s. for another week along with oral diuretics. The L III tracing (Fig. 9) shows ventricular tachycardia, and L I and V 3 show coupled rhythm (Fig. 10). Two g. of potassium was given in 500 ml. of glucose and the tracing returned to normal (Fig. 11). After one week of stoppage of digitalis the patient again developed ventricular tachycardia. This must be due to the disease itself. Incidentally, the serum potassium was found to be 5 mEq/l., suggesting again that the serum level does not indicate the tissue content of potassium.

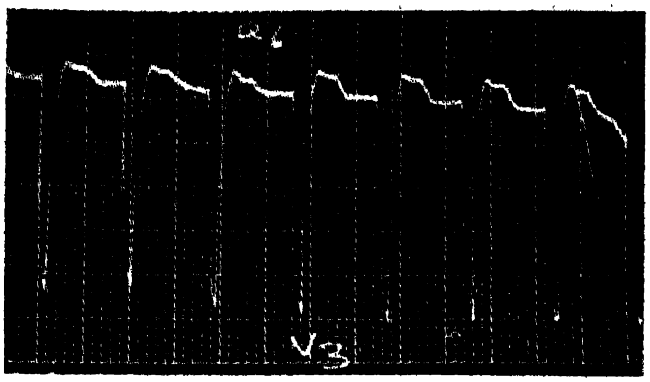

FIG. 5—SHOWING SUPRAVENTRICULAR TACHYCARDIA (? NODAL)

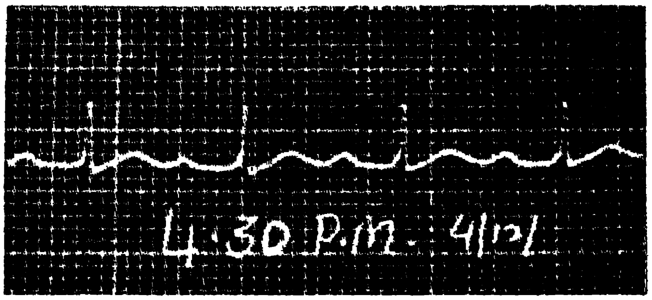

FIG. 6—SHOWING PROLONGATION OF P.R. INTERVAL

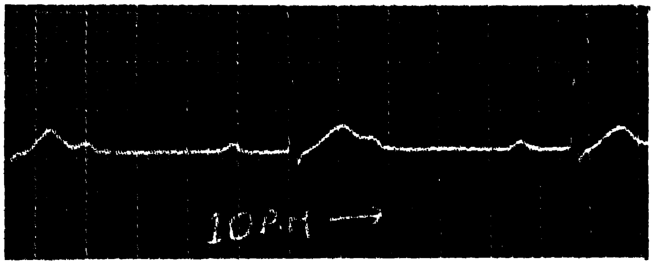

FIG. 7—SHOWING 2 :1 BLOCK

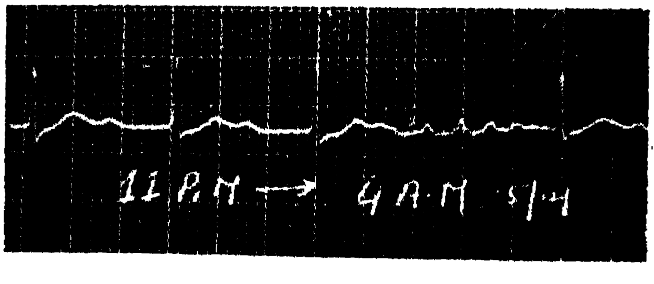

FIG. 8—SHOWING 4 :1 BLOCK

FIG. 9—SHOWING VENTRICULAR TACHYCARDIA

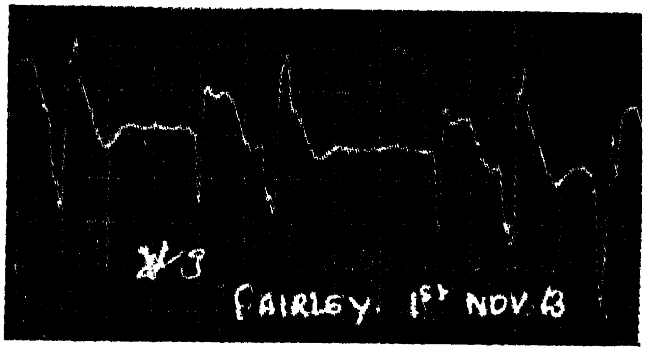

FIG. 10—SHOWING COUPLED RHYTHM

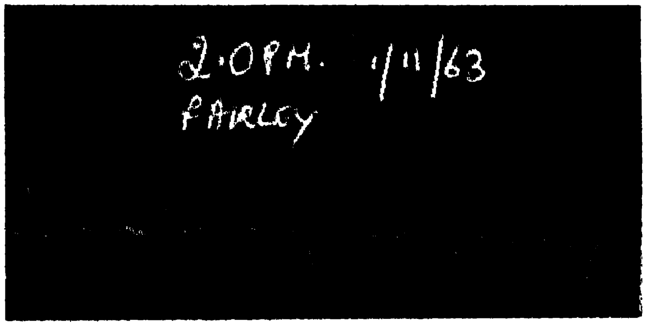

FIG. 11—SHOWING NORMAL RHYTHM AFTER POTASSIUM THERAPY

In spite of difficulties one must always look for some pointers. Apart from the high index of suspicion, the characteristic rhythm changes like supraventricular tachycardia with block, coupled rhythm, bi-directional tachycardia are to be sought. These changes are transient and varying. In some cases the less common features like visual and neurological manifestations have to be directly questioned.

TREATMENT

The incidence of the toxicity could be reduced if pure preparations are used, and the minimal effective dose is used with regular observations both by the patient and the doctor. Special care in the use of parenteral therapy is essential.

Curative—1. Discontinuance of the drug as in all toxicity states.

2. Withholding the diuretic measures.
3. Administration of potassium, either orally or intravenously in emergency.
4. Anti-arrhythmic agents like procainamide or quinidine, to be used where necessary.
5. Use of chelating agent like EDTA (di- or tri-sodium salt).

The oral dose of potassium is 3 to 4 g. Renal condition is important before deciding on intravenous therapy. Recent studies show that the EDTA is useful in the treatment by virtue of its producing hypocalcaemia. The effect is found to be transient and the drug may be used along with potassium. 3 g. of the drug can be given safely during a period of 20 minutes (intravenously).

CONCLUSION

Digitalis is a potent but dangerous drug especially in the presence of oral diuretics. Hence the nesessity of proper care in the use of the drug which is only one of its kind so that it is not lost to medicine.

INFECTIOUS CROUP

A Study of 257 Cases

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Croup is a paediatric emergency. It is characterised by difficult and noisy respiration and is often accompanied by cough and hoarseness because of varying degrees of laryngeal obstruction resulting from oedema and/or spasm. Such a syndrome can also be produced by a foreign body or a tumour in the subglottic region, but commonly it is due to infection of the larynx and trachea. The discussion here will be confined to infectious croup which is due to an inflammatory disease of the upper respiratory tract. The cases may present with a varying degree of severity—slight hoarseness and cough on the one hand to a restless, cyanotic infant struggling for breath with marked retractions of the intercostal spaces on the other extreme.

MATERIAL AND METHOD

The material of this study consisted of 257 cases of infectious croup at the D.N.P. Bagla Infectious Diseases Hospital during the years 1962-63. They constituted 6 per cent of total yearly admissions to this hospital.

All cases with noisy breathing, hoarseness and cough with signs of inflammation in the larynx or tracheobronchial tree were included in this study.

Information regarding age, sex, religion, immunisation status, date and time of onset of symptoms, degree of toxaemia and respiratory obstruction was noted. The upper respiratory tract and the lungs were carefully examined. A bacteriological study with smear examination and culture was done in each case. Those cases which did not show growth of any bacterial pathogen, but had a consistent clinical picture, were presumed to be of viral origin. We do not have the facilities of virological investigations, so a definitive study in such cases was not possible. The occurrence of complication was noted. The patients were followed up for 4 to 6 weeks after discharge and were asked to report if anything untoward happened later.

OBSERVATIONS

Different clinical observations are presented in Tables 1 to 7.

TABLE 1—SHOWING AETIOLOGICAL FACTORS

Aetiology	No. of cases	Percentage
C. diphtheriae	69	26·8
H. influenzae B	20	7·7
Viral	168	65·5
Total ...	257	100

TABLE 2—SHOWING PERCENTAGE INCIDENCE ACCORDING TO AGE GROUPS (YEARS)

Aetiology	0—2	Above 2 and up to 5	Above 5 and up to 12
C. diphtheriae ...	60·1	30·6	9·3
H. influenzae B ...	30·0	55·0	15·0
Viral	63·1	30·3	6·6

TABLE 3—SHOWING SEX INCIDENCE

Aetiology	Percentage	
	Male	Female
C. diphtheriae	61	39
H. influenzae B	60	40
Viral	68	32

TABLE 4—SHOWING PRESENTING SYMPTOMS

Symptoms	Percentage		
	C. diphtheriae	H. influenzae B	Viral
Stridor	100	100	100
Cough	96	90	96
Fever	92	100	90
Hoarseness	22	25	25
Aphonia	10	20	12
Intercostal retraction ...	68	80	42
Inability to take feeds ...	34	50	26
Nasal discharge	4	20	75

TABLE 5—SHOWING DURATION OF ILLNESS

Duration of illness on admission	Percentage		
	C. diphtheriae	H. influenzae B	Viral
Less than 24 hours	25	80	12
24 to 48 hours	63	20	58
2 to 4 days	12	—	30

TABLE 6—SHOWING DEGREE OF SEVERITY

Aetiology	Mild		Moderate		Severe		Fatal		Total no. of cases
	No.	%	No.	%	No.	%	No.	%	
C. diphtheriae ..	3	4·4	17	24·6	33	47·8	16	23·2	69
H. influenzae β ...	2	10·0	5	25·0	8	40·0	2	25·0	20
Viral	56	33·3	63	37·5	41	24·4	8	4·8	168

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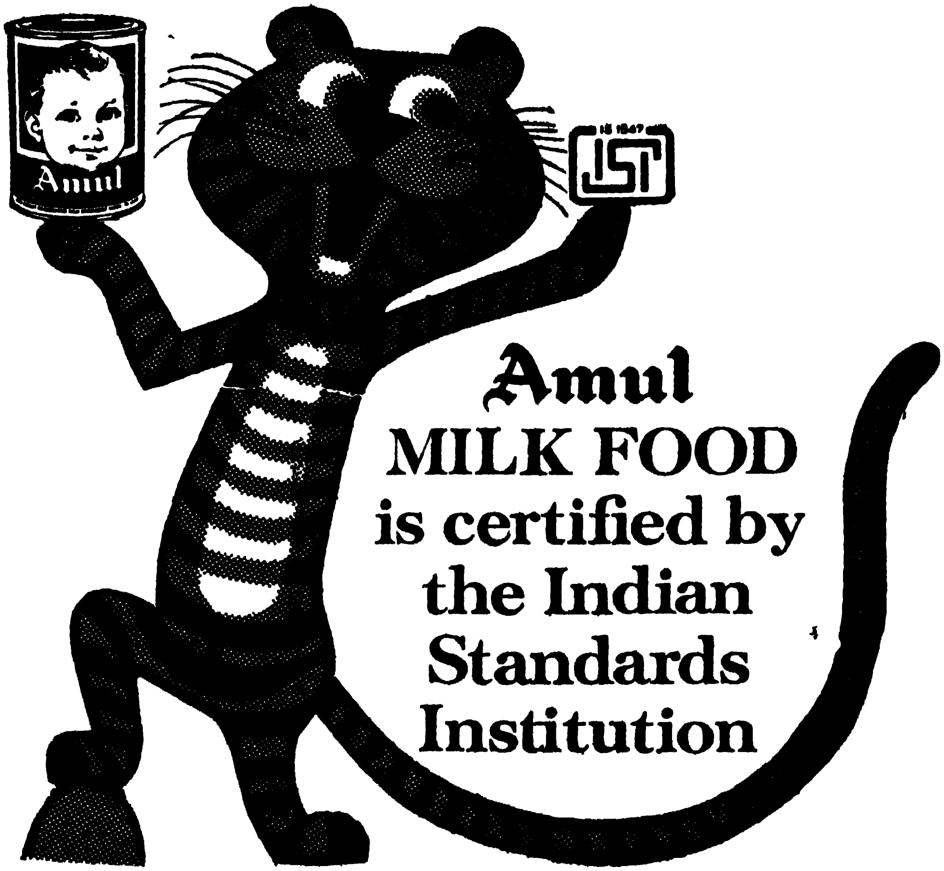

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TABLE 7—SHOWING COMPLICATIONS

Aetiology	Nature of complication	No. of cases	Percentage (groupwise)
C. diphtheriae	Myocarditis	7	10·1
	Obstruction to larynx	69	100
	Secondary bronchopneumonia	8	11·5
	Palatal paralysis	4	5·8
	External rectus paralysis	2	2·9
	Pharyngeal paralysis	2	2·9
	Laryngeal paralysis	1	1·4
H. influenzae B	Crusting of trachea	6	30·0
	Subcutaneous emphysema	1	5·0
Viral	Crusting	21	12·5

N.B.—Some patients had more than one complication

Seasonal variations—The number of cases of different types of croup seen in each month were analysed. Although the cases of croup were seen all the year round but largest number of cases (44·6 per cent) of diphtheria occurred in the months of August, September and October while largest number of cases of *H. influenzae* (75 per cent) and viral (78 per cent) croup were seen in the months of November, December and January.

Immunisation status—None of the patients in this series was immunised with triple antigen (DPT) or diphtheria toxoid alone.

Mortality—There were 29 deaths (11·2 per cent) in this series of 257 cases. Analysing these groupwise, 16 deaths (23·2 per cent) occurred in diphtheritic cases, 5 (25 per cent) in influenzal croup, and 8 (4·8 per cent) in viral cases.

The mortality was found to be higher in those patients which were admitted late in the hospital, in infants and those patients whose nutrition was poor.

DISCUSSION

The commonest cause of croup is viral infection. There are two proved becterial agents—*C. diphtheriae* and *H. influenzae B*—which cause croup. In the present series of 257 cases, studied over a period of two years, 168 cases (65·5 per cent) were viral, 69 cases (26·8 per cent) were diphtheritic and only 20 cases (7·7 per cent) were due to *H. influenzae* infection. In a study of 347 cases, Raba (1948a) found only 50 (14·7 per cent) cases due to bacterial aetiology, 28 cases due to *H. influenzae B* and 22 due to *C. diphtheriae*. In the remaining 297 patients (86 per cent) a constantly occurring bacterial pathogen could not be isolated on ordinary culture, but similarity of symptom-complex, clinical course and living morbid pathology led him to speculate that this latter group of cases had a viral aetiology. In the present series the cases of diphtheria were more numerous as compared to any Western series. It is understandable as diphtheria is a common condition in India while it has nearly been wiped out from Western countries.

The following viral agents are known to cause croup in children: Parainfluenza type 1 (haemadsorption virus type 2; HA-2), parainfluenza type 2 (CA virus), parainfluenza type 3 (haemadsorption virus type 1; HA-1), influenza A virus, adenovirus, C.C.A. virus, ECHO 11, and respiratory syncytial (RS) virus.

Chanock (1957) and Beale *et al.* (1957), working independently, isolated a virus from children suffering from croup, which was called croup associated (CA) virus by the former and acute laryngotracheobronchitis (A.L.T.B.) virus by the latter. It has now been named as parainfluenza type 2 virus. Probably the commonest virus causing croup is parainfluenza type 1.

During an epidemic of Asian influenza in Australia, Forbes (1958) observed 127 cases of croup in association with influenzal infection. A study by Vargosko *et al.* (1959), during the 1957 Asian influenza epidemic, showed evidence of viral infection in 64 per cent of 47 cases with croup. The incidence of aetiologic types of infection was: parainfluenza type 1 (HA-2) 36 per cent; Asian influenza virus 19 per cent; the remaining 9 per cent was caused by adenovirus, parainfluenza type 2 or type 3. Thus in spite of the Asian influenza epidemic, parainfluenza type 1 was the most common cause of laryngotracheobronchitis in their series.

Many children may have more than one attack of viral croup, but the severity of the attacks lessens as the child grows older. What was described as spasmodic croup in the past is really due to viral infection. This form of croup was described as developing suddenly at night, tending to be recurrent and usually associated with minor respiratory infection. It was presumed to be due to allergy or immaturity of the larynx and to occur in the nervous type of child. Although a major portion of laryngeal obstruction in this from of croup is due to spasm, there is also some degree of subglottic oedema. Cramblett (1960) stated that there was increasing evidence that laryngeal spasm is triggered by and associated with preceding viral infection of the upper respiratory tract.

Various pathogenic bacteria, including β Haemolytic streptococci have been implicated, but most of them are now regarded as secondary invaders (Krugman and Ward, 1960) ; they may however add to the severity of the disease (Morgan and Wishart, 1947).

In the present series the cases of diphtheria and viral infection occurred mainly in infants (6 months to 2 years), while *H. influenzae* croup was commonest in children between 2 and 5 years of age. Cramblett (*loc. cit.*) found the majority of cases of croup, in children between the ages of 3 months and 3 years, *H. influenzae* and diphtheritic croup.

The incidence was highest in male in all types of croup (diphtheritic 61 per cent, influenzal 60 per cent, and viral 68 per cent). Rabe (1948a) and Cramblett (*loc. cit.*) also reported a significantly higher incidence of infectious croup among male patients. The cause of this higher incidence among males is not known.

In the present series 44·6 per cent of cases of diphtheria occurred in the three months from August to October, while 75 per cent of *H. influenzae* and 78 per cent of viral croup occurred in the months of November, December and January. As there is an increased incidence of all types of respiratory infections during the winter months, it is understandable that the bulk of cases of croup is also likely to occur then.

It is not known as to why only some children develop croup when a large number may get the same viral infection. It has been postulated in the past that this predisposition may be due to an anatomically defective larynx or immaturity of the larynx, but there is no definite evidence to prove that this is so.

It has also been thought from time to time that allergic factors may also play some role in the causation of croup.

The analysis of clinical features disclosed characteristic features in different groups of cases. In diphtheria signs of upper respiratory infection precede the characteristic membrane formation by 3 to 4 days. Most of the cases of diphtheritic croup were admitted within 24 to 48 hours of the onset of symptoms because the laryngeal involvement gives rise to signs of respiratory obstruction and which compels institution of an early treatment. The white cell count ranged from 12 to 17 thousand per c.mm. with 75 to 80 per cent polymorphs.

The cases of *H. influenzae* croup have a rapid onset. Only a few hours after the manifestation of initial symptoms, the patients appear seriously ill, with high temperature and marked stridor. The child leans forwards struggling to get air in the lungs. The examination reveals marked supraglottic oedema and the epiglottis is fiery red and markedly swollen (stiff epiglottis). There may be exudates on the tonsils. It is appropriate to repeat Rabe's (1957) warning that vigorous attempts to depress the tongue to see the epiglottis should not be made since this manoeuvre can lead to sudden permanent respiratory arrest. The death in cases of *H. influenzae* croup may sometimes occur within 24 hours. Because of marked respiratory obstruction tracheostomy was required in 60 per cent (12) cases. The white cell counts ranged between 22-25,000 per c.mm. with 84 to 95 per cent polymorphs. Death occurred in 25 per cent of cases.

In croup of viral origin there was an initial history of upper respiratory tract infection and some irritability and restlessness. Many of the attacks initially began during the night, the so called spasmodic croup. The degree of toxaemia was not as marked as in diphtheritic or *H. influenzae* croup. The examination revealed mild supraglottic and moderate to marked subglottic oedema. The secretions were thin at the onset but later dried up to form crusts. Tracheostomy was required when the involvement of upper respiratory tract was extensive. Thus in Rabe's (1948b) series tracheostomy was performed in 0·6 per cent cases of laryngitis, 16·3 per cent of cases of laryngotracheitis and 47 per cent of cases of laryngotracheobronchitis.

The severity of any given case was found to depend on : (a) the extent of involvement of the respiratory tract (i.e., tracheitis or laryngotracheobronchitis), (b) on the degree of obstruction, (c) on the age of the patient (more serious in infants), (d) causative organisms and (e) delay in starting treatment.

MANAGEMENT

The main principles in the management of children with infectious croup are outlined below :

General care—The child is put to bed and is kept in a quiet ward. The various diagnostic and therapeutic procedures are kept to a minimum so as not to disturb the child. It is needless to say that good nursing care and sympathetic approach towards the child are essential.

Sedation is not advisable in a majority of children, as it would depress the respiratory centre still further. An important point to remember is that a child may be restless due to anoxia and what he really requires is tracheostomy and not sedation. In cases, where restlessness is not due to anoxia, phenobarbitone 6 mg./Kg. may be given intramuscularly with care.

Humidity—High atmospheric humidity, up to 95 per cent, is desirable as it is soothing to the dry irritated mucosa and it lessens the chances of crusting of secretions. Although cool mist is preferable to steam, in most of the places in our country only steam may be available. A large pan filled with water is allowed to boil on a stove in the room. It will provide the required humidified atmosphere.

Fluids—Because of dyspnoea, fever and failure to give water to these children, they are liable to become dehydrated. Dehydration also causes increased crusting of secretion and thus contribute to respiratory obstruction. Initially the fluids may have to be given by intravenous drip, the amount depending on the age, size and degree of dehydration. After initial correction of dehydration the required amount of fluid is given orally. In all cases an intake output chart is maintained.

Bronchodilators—When spasm is present, which can occur in viral and *H. influenzae* infections, aminophylline is given. The dosage for this drug by intravenous route is 10-12 mg./Kg./24 hours and rectally the dose is double of intravenous dose. Oral aminophylline is not so effective.

Antibiotics—In cases of diphtheria, penicillin is given intramuscularly in doses of 25,000 to 50,000 units per Kg. body weight in 24 hours (divided in 4 or 6 equal doses). For *H. influenzae* and viral croup, a tetracycline (20-40 mg./Kg./24 hours orally or 12 mg./Kg./24 hours parenterally) or chloramphenicol (50 mg./Kg./24 hours orally) is given. Although chloramphenicol is used most extensively in *H. influenzae* croup, there are no controlled studies to indicate that it has any particular advantage over tetracycline. Cramblett (*loc. cit.*) stated that he has never encountered any strain of *H. influenzae* which was resistant to tetracycline *in vitro*. Krugman and Ward (*loc. cit.*) recommended that a combination of penicillin and chloramphenicol should be given to all severe cases.

Cases of diphtheritic croup are given diphtheria antisera (ADS) as early as possible after testing for sensitivity.

Patent airway—The maintenance of a patent airway is of utmost importance. In cases with large amounts of secretions endoscopic aspiration of exudate and tracheal crust is required. If there is respiratory obstruction tracheostomy should be done and repeated suctions carried out through it.

Steroids—The anti-inflammatory effect of these agents reduces oedema and thus help to relieve obstruction. They also improve the general condition of patients who are severely ill. But if the obstruction is marked a tracheostomy takes precedence over all other treatment.

Wetting agents and fibrinolytic enzymes—Their role is dubious. Maintenance of proper hydration and humidity are more effective in preventing the secretions from drying and in helping their expectoration.

SUMMARY

A group of 257 cases of infectious croup, seen over a period of two years, has been studied. In this series the majority of cases were of viral origin (65·5 per cent) followed by diphtheria (26·8 per cent) and *H. influenzae* accounting for only 7·7 per cent of cases.

Diphtheria and viral croup were noted to occur more commonly in infants while *H. influenzae* was commoner in children aged 2 to 5 years. There was a significant preponderance of males over females in all types of croup.

Cases of diphtheria were commonly encountered in the months of August, September and October, while majority of cases of *H. influenzae* (75 per cent) and viral (78 per cent) croup were seen in the three months from November to January.

It was found that cases of diphtheria and *H. influenzae* had the highest mortality—being 23·2 and 25 per cent respectively.

The complications encountered in cases of diphtheritic croup were myocarditis, obstruction to larynx, secondary bronchopneumonia, palatal paralysis, external rectus paralysis, pharyngeal and laryngeal paralysis. In *H. influenzae* and viral cases the main complication was crusting of secretions in the tracheobronchial tree. One case of *H. influenzae* croup developed subcutaneous emphysema.

The clinical features and the management of the cases have been discussed.

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CASE NOTES

PULMONARY AND GASTRIC ASPERGILLOSIS

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Aspergillosis—localised and disseminate forms—is caused by the Aspergillus species. *Aspergillus fumigatus* commonly is identified morphologically and culturally as responsible for bronchopulmonary lesions. *Aspergillus niger, versicolor, nidulans* and *flavus* species have also been identified in these lesions. It is a common contaminant of laboratory materials and is to be eliminated even if the diagnosis is based on cultural findings. Single isolations have no diagnostic importance unless repeatedly recovered. The recognition of the fungus under the microscope is not beset with any difficulty as the hyphae which may be long and of medium width usually about 8-12 μ are septated, showing prominent branching but may be tree-like. Clamydospores or very rarely conidiospores may be seen in a bronchial lumen or inside a vessel. Conidiospores with terminal vesicle, stigmata and dark peripheral spores in chains may be encountered. The demonstration in the lesions or in sputum repeatedly of branching hyphae is conclusive proof of infestation. Very often one observes aspergillus colonies occluding the lumen of the bronchus.

Aspergillosis is viewed as exogenous infection. The respiratory tract is the most common site of involvement and the lung is the usual site from which dissemination takes place in systemic aspergillosis. Aspergilli are regular inhabitants of the soil and are pathogenic to man and are ubiquitous. Pigeons, parrots or birds in captivity constitute the medium of exposure. Many, however, doubt the existence of human aspergillosis. It has been the convention to reject diagnosis of aspergillosis and admit only as suspect when all other sources are eliminated. Many cases of aspergillosis have been reported in France, particularly, in individuals exposed to massive doses of fungous spores such as squab feeders, fur cleaners, and agricultural workers. All races are affected. Men are most commonly infected. Exposure to spores through occupation is a contributory factor. Involvement of the bronchi and lung is probably the most important clinical manifestation of aspergillosis. It may be superficial and graze the bronchial epithelial surface or affect the parenchyma and reside in the alveoli and plug the bronchial lumen in the form of aspergilloma or invade a vessel lumen and destroy contiguous areas of lung through infarction. The pulmonary lesions may be acute or chronic and resemble bronchopneumonia or abscess or tuberculosis. These infections clinically and roentgenologically simulate tuberculosis closely. Prognosis is poor when there is massive involvement of lung parenchyma with abscess formation.

The first case of clinical aspergillosis was recorded 60 years ago, although the first fatal case of the same was reported by Virchow (1856). Renon (1897) reviewed this condition and since then many papers have been published. Recently, Monad and Meyer (1957) pointed to its rather common occurrence. Meyer *et al.* (1956) reviewed 21 cases of aspergilloma. Mycotic infections are alarmingly on the increase in recent years in cases receiving antibiotics, nitrogen mustard chemotherapy and folic acid antagonists. Disseminate mycotic lesions are a feature in cases under folic acid antagonists or A.C.T.H. therapy. Profound leukopenia induced by antileukaemic drugs appear to increase the susceptibility to infection. Cortisone and antibiotics reduce host resistance to aspergillosis in animals and pulmonary aspergillosis occurs as a complication of other diseases. Aspergillosis is far more likely to occur in patients with disturbances of reticulo-endothelial system. Lymphomas and leukaemias are secondarily associated with mycosis. Many of these patients had received heroic doses of steroids for 6 weeks or antibiotics in massive doses. Most of them developed leukopenia and neutropenia.

Clinical and pathological findings in two cases, one each of pulmonary and gastric aspergillosis which were under antibiotic and steroid therapy are recorded to alert the clinicians of this complication.

CASE REPORTS

CASE 1 (PULMONARY ASPERGILLOSIS):

V.R., Hindu male, aged 6 years, was admitted on 16-6-1963 in King George Hospital, Visakhapatnam, for fever and passing blood and mucus in stools. The patient was unconscious and had convulsions two days prior to admission. He was irritable. Tongue was clear and moist. Physical examination of the systems revealed nothing remarkable.

Cerebrospinal fluid was clear; Rate—40 drops per minute. Pandy's test—Negative. Proteins—40 mg. per cent, sugar—82 mg. per cent, chlorides—660 mg. per cent, cells—3 per cmm.

Total W.B.C. count—8,900 per cmm. with polymorphs 70 per cent, lymphocytes 28 per cent and eosinophils 2 per cent.

Haemoglobin—8 g. per cent.

Blood culture for enteric group of organisms —Negative. Widal test—Negative.

Faeces—Red blood cells and pus cells were seen.

The patient was treated with capsules of chloromycetin. Since there was persistent distension of the abdomen, laparotomy was performed under general anaesthesia on 20-6-1963. Jejunal loops appeared congested and bore ulcers. The intestines were distended. There was neither perforation nor obstruction in the intestine. The wound was closed in layers. The patient was put on penicillin, chloromycetin and vitamin B complex. The patient continued to run temperature ranging between 103° and 104°F and expired on 29-6-63.

Salient autopsy findings inclusive of histology (3428)—Besides congestion of the meninges there was nothing particular in the central nervous system. The right lung weighed 110 g. and the left lung weighed 120 g. The lower lobes were not crepitant. They appeared to be solid and cut section showed marked congestion and haemorrhage and minute yellow zones, all suggestive of bronchopneumonia. Sections of the lungs (1420-A-D/63) showed multiple areas of necrosis in the centre of which was the colony of aspergillus filaments with no cellular reaction and bordering this was seen compressed lung parenchyma (Figs. 1 and 2, *vide* Plate). These clusters of aspergillus filaments were in radiating manner (Fig. 3, *vide* Plate).

Heart showed nothing remarkable. Liver weighed 470 g. and was soft and pale. Sections showed fatty change. Spleen weighed 45 g. and was congested. Sections showed haemorrhages and aggregates of mononuclears. Each kidney weighed 50 g. and both were congested. Both the adrenals showed haemorrhages. Coils of intestines were adherent to each other being glued together by pus. Small intestines showed extensive areas of membranous inflammation and the lumen contained large plaques of denuded mucous membrane, some of which when picked up by forceps unmasked ulcers beneath. Sections from the intestines showed fibrinoid necrosis with round cell infiltration of the mucosa and deeper layers. From the necropsy findings a diagnosis of aspergillus bronchopneumonia was made.

CASE 2 (GASTRIC ASPERGILLOSIS):

B.A., Hindu male, aged 33 years, was admitted in King George Hospital, Visakhapatnam, on 10-6-63 for jaundice, pain in the abdomen and fever of 2 months' duration. Oedema of feet, ascites, and anaemia were observed. Liver was palpable one finger below the right costal margin and was firm and tender.

Total W.B.C. count—8,500 per cmm. with polymorphs 68 per cent, lymphocytes 12 per cent, monocytes 12 per cent and eosinophils 8 per cent. Serum van den Bergh—Positive in one minute. Serum bilirubin—24 units. Thymol turbidity test—4 units. Zinc sulphate test—7 units. Serum alkaline phosphatase—10 K.A. units (10-6-63) and 34 K.A. units (13-6-63).

The patient was put on liver extract, vitamin B complex, vitamin C and intravenous glucose. Aureomycin and cortisone were administered. On 1-7-63 he became unconscious, his pulse was imperceptible and respirations irregular. On 4-7-63 the patient expired.

Salient autopsy findings inclusive of histology (3828)—Yellowish discoloration of the skin and mucous membranes was observed. Peritoneal cavity contained 50 oz. of bile-stained fluid; left pleural cavity contained 16 oz. of bile-stained fluid. Lungs showed hypostatic congestion. Brain and heart showed nothing remarkable. Spleen weighed 210 g. and was soft and diffluent. Liver was reduced in size and soft. Sections showed diffuse necrosis. Sections of kidneys showed bile casts occluding the renal tubules. Haemorrhages were seen over the mucosa of the stomach. Sections of the stomach showed denudation of the mucosa and penetration of the filaments of aspergillus deep into the muscular layers (Figs. 4 and 5, *vide* Plate). Some of the branching hyphae of the fungus were seen occluding the lumen of the blood vessels. The postmortem findings were conclusive of subacute infective hepatitis complicated by aspergillosis of the stomach.

COMMENT

Both the case reports confirm the findings of the earlier observers that aspergillosis in the human is invariably detected at necropsy. The antibiotics administered to both the patients and the steroids to one should naturally have promoted the seedling of the fungus in the lung and the stomach. The poor or no response to leucocytic proliferation observed in typhoid and infective hepatitis is yet another factor for easy entry of the fungus into these viscera in these cases. The multiple microabscesses in the lungs illustrate the fulminant nature of pulmonary aspergillosis. In both the cases the fungus did not excite any cellular reaction. It would be wise to bear in mind the unforeseen threat of visceral fungal infections under moderate or heavy antibiotic or steroid therapy.

SUMMARY

Two cases, one each of pulmonary and gastric aspergillosis, diagnosed at necropsy are recorded and the need of vigilance on patients under antibiotic and steroid therapy is stressed.

The literature on aspergillosis in man is briefly reviewed.

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CHRONIC PANCREATITIS WITH PANCREATIC CALCIFICATION AND DIABETES MELLITUS

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Diffuse pancreatic calcification is seen radiologically in nearly 10 per cent of cases of chronic pancreatitis. The various clinical features, e.g., pain in the abdomen, steatorrhea, jaundice, calcifications and diabetes mellitus usually appear very late in the course of the disease. Chronic pancreatitis occurs commonly in the males in the fourth or fifth decades and is usually associated with a history of alcoholism or some diseases of the neighbouring structures.

The case reported here is that of a 26-year-old female who presented with diabetes mellitus only without any previous history of illness.

Case Report

M.N.L., a 26-year-old married Hindu female, was admitted to the B. S. Medical College Hospital, Bankura, with polyuria, polyphagia, polydipsia, loss of weight and generalised pruritus for one year and a half and amenorrhoea for one year. She noticed gradual swelling of the abdomen and oedema of legs for the last four months. There was nothing contributory in the past or family history. She had no treatment before admission in this hospital.

The patient was thin and emaciated. There was evidence of free fluid in the abdomen and oedema of the legs. There were no significant abnormalities in other systems.

Investigations—Urine: Sugar + + +, acetone nil. Blood: Hb. 10 g. per cent, sugar 532 mg. per cent, urea 36 mg. per cent, N.P.N. 28 mg. per cent, serum cholesterol 223 mg. per cent, total protein 7 g. per cent, serum albumin 4·2 g. per cent, serum globulin 2·8 g. per cent, calcium 10 mg. per cent, phosphorus 4 mg. per cent, serum bilirubin 0·4 mg. per cent, serum alkaline phosphatase 3·1 (Bodansky unit), zinc sulphate turbidity 4 units. Stool: No abnormality detected. Skiagraphy: Chest—normal; abdomen—diffuse pancreatic calcification and generalised haziness of abdomen suggesting fluid.

Treatment—The treatment was started with soluble insulin and the dose was raised up to 200 units daily but the patient was still passing sugar in the urine and blood sugar at that time was 354·4 mg. per cent. Then in addition to insulin metformin hydrochloride (glyciphase) 300 mg. daily was given and within a week's time the blood sugar came down. Oedema and ascites were controlled by hydrochlorothiazide (dichlotride) 150 mg. daily. Other treatments given were ethylestrenol (orabolin) 6 mg. and vitamin B complex daily.

Progress—The patient progressed well during the course of the treatment. At the time of discharge from the hospital diabetes was controlled. Patient gained weight and was free from ascites or oedema.

Discussion

The incidence of diabetes mellitus in chronic pancreatitis varies in different series, highest was 51 per cent (King, 1949) and the lowest 7·6 per cent (Fitzgerald *et al.,* 1963).

It is very uncommon in case of chronic pancreatitis with diffuse pancreatic calcification to present only with hyperglycaemia and glycosuria without any manifestation of pancreatic deficiency, and it may be explained by involvement of islet cells of the pancreas only.

Ascites and oedema may be due to local pressure effects over the portal vein or its tributaries by the calcified pancreas, but there is a possibility to latent cirrhosis of the liver though there was no history of alcoholism and blood biochemical examinations were normal. Diabetic nephropathy, hypoproteinaemia or severe anaemia as a cause of ascites and oedema were excluded by normal blood picture. The insulin oedema usually appears very early in the course of the treatment with soluble insulin and mainly marked over the face. This patient had ascites and oedema even before the treatment was started with insulin. However, it was controlled by oral diuretics. The next interesting feature of this case was that she was insulin resistant requiring 200 units of soluble insulin daily along with glyciphase. She never had diabetic ketosis of acetonuria though her blood sugar was very high and she had no treatment previously. The cause of the pancreatic calcification remained undiscovered but it may be related to hypercholesterolaemia. This patient had high blood cholesterol (normal level in this area being 100-200 mg. per cent). But again high cholesterol may be the effect of uncontrolled diabetes. The possibility of hyperparathyroidism was excluded by normal blood calcium, phosphorus and serum alkaline phosphatase level.

SUMMARY

Pancreatic calcification presenting only with resistant diabetes in a young female patient is reported.

The cause of ascites and oedema remained obscure and the possibility of local pressure and latent cirrhosis is suggested.

High cholesterol level may be a possible cause of pancreatic calcification.

ACKNOWLEDGMENT

The author is thankful to Dr. D. Raymahasaya, Principal and Superintendent, B. S. Medical College Hospital, Bankura, for permission to report this case and Dr. S. P. Sarkar, Assistant Professor of Radiology, for the x-ray reports.

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SADDLE EMBOLISM AT THE AORTIC BIFURCATION IN A CASE OF MITRAL STENOSIS

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The occurrence of saddle embolism at the bifurcation of the aorta resulting in sudden arterial occlusion at this site is one of the most dramatic and catastrophic emergencies in medical practice. Banowitch and Ira (1928) were the first to stress the importance of mitral stenosis as an aetiological factor. The onset of auricular fibrillation leading to dislodgement of a thrombus from the auricular appendage is the exciting cause in most of these cases. This serious and often fatal complication may also occasionally arise from mural thrombi in myocardial infarction, during or soon after mitral commissurotomy or cardiac catheterisation. Schein *et al.* (1956) state that very rarely it may be the result of a detached plaque from an atheromatous aorta, getting impacted distally at its bifurcation.

209 cases of aortic embolism at its bifurcation were reported uptil 1952 (Wilkinson, 1952) and in 75 per cent of these cases, it had proved fatal. Because of such a high mortality with conservative medical treatment and due to recent advances in vascular surgery offering a better prospect, provided the surgery is carried out within a few hours, it becomes extremely important to diagnose these cases soon after the occurrence. Very few cases of this uncommon condition have been reported from this country (Basu and Dass, 1956; Singh and Gupta, 1958). A case of saddle embolism at the aortic bifurcation occurring in a case of mitral stenosis precipitated by auricular fibrillation is being reported.

CASE REPORT

K.C., 22 years of age, farmer by occupation, was admitted with the diagnosis of rheumatic heart disease with mitral stenosis and regurgitation with congestive heart failure. Two years before admission he started having palpitation and breathlessness on moderate exertion and these symptoms were progressive since then. At the time of admission he was breathless even at rest. He was also complaining of general weakness and was unable to do any work because of palpitation and dyspnoea. There was no history of any pain in the chest, haemoptysis, or epistaxis suggestive of any embolic phenomenon.

Past history of joint pains or chorea was not available.

Physical examination—He was moderately built and nourished. Some puffiness of the face and oedema of the feet and legs were present. The neck veins were prominent and I.V.P. was raised. There was neither clubbing nor cyanosis. Respiration was 24 min. Pulse was 90/min., regular and poor in volume. Blood pressure 120/90 mm. of Hg. The precordium was bulging and there was a diffuse cardiac impulse in the left parasternal region. Apex beat was in the fifth intercostal space outside the midclavicular line. Both the heart sounds were audible in all the areas. Mitral first sound was sharp and loud and the pulmonary second sound was also markedly accentuated. Both systolic and diastolic murmurs were present in the mitral area. Liver was palpable four fingers below the costal margin and the lungs showed signs of pulmonary congestion.

Investigations—Haemoglobin was estimated at 12 g. per cent. Total leucocyte count 11,200/cmm. E.S.R. 12 mm. 1st hour (Westergren). Urine and stools revealed no abnormality. Blood urea 63 mg. per cent. S.T.S. was negative. E.C.G. mitral P-wave with right ventricular preponderance.

Radiological examination—Increased transverse diameter of the heart with mitral configuration. Barium study of oesophagus showed left auricular enlargement.

Treatment and progress report—The patient was treated on usual lines for congestive heart failure with rest, salt-free diet, digoxin and diuretics. He improved and started moving about. One day while going to the bathroom he suddenly felt pain in the hypogastrium, which was followed by severe agonising pain in both the lower limbs along with marked weakness. He fell down and could not get up. He also complained of numbness of both the feet and legs.

On examination, there was complete loss of power in all the muscles of the legs and feet. The movements at the toes and ankles were not possible, but flexion and extension movements at the knees though weak were present. All the sensations up to the knees were lost. The deep reflexes were absent. Both the feet and the legs up to the upper third were cold. The pulsations in the femorals, popliteals, posterior tibials and dorsalis pedis were absent. At that time the pulse was irregularly irregular and the heart was fibrillating. Diagnosis of auricular fibrillation leading to saddle embolism of the bifurcation of the aorta was made. Emergency operation of embolectomy was carried out. On opening the abdomen, pulsations at the lower end of the aorta and the iliac vessels were found to be absent. A big clot from the aortic bifurcation extending into both the common iliac vessels was removed. Pulsations in both the femorals and popliteals returned immediately and the legs became warm but the whole of the left foot and distal half of the right foot remained cold. He was put on oral anticoagulant therapy along with vasodilator drug (priscol), broad spectrum antibiotics, vitamins B_1 and B_{12}, I.V. glucose drip and rest to the lower limbs. The numbness and coldness of the feet and lower part of the left leg persisted so paravertebral sympathetic block was given. The patient was well on the way to recovery but on the third post-operative day, the patient suddenly became breathless and cyanosed. Oxygen inhalation and artificial respiration were started but he expired within a few minutes and it was thought that he had a massive pulmonary infarction.

DISCUSSION

Though peripheral embolisation is one of the fairly common complications of mitral stenosis particularly when it is associated with auricular fibrillation, aorta is the least common vessel to be involved (Friedberg, 1956) and so saddle embolism at the aortic bifurcation is quite rare. Haimovici (1950) found that out of 330 cases of arterial emboli, aorta was the site of impaction only in 9 per cent cases. Belcher and Somerville (1955) while reviewing 430 cases of mitral stenosis with embolic complication, found that aortic bifurcation was involved in 7 per cent cases.

The diagnosis of acute embolism of the aortic bifurcation with its classical picture of sudden and dramatic onset, complete arrest of circulation in the legs, resulting in intense and excruciating pain in both the lower limbs coupled with marked degree of muscle weakness, complete loss of sensations, coldness of extremities and absence of pulsations in the popliteal and femoral vessels, should present no difficulty. This is the usual classical picture resulting from saddle embolism. Read *et al.* (1960) state that the clinical picture depends upon completeness of the plugging of the lumen, degree of arterial spasm, embolus moving down the arterial tree, extent of secondary thrombosis and the efficiency of collateral circulation. Variation in the interplay of these factors results in the variability of the clinical picture. They describe two other types of cases in addition to the classical acute one :

(1) Sub-acute or insidious type where the circulation is incompletely obstructed and the onset is slow and gradual. There is no immediate threat to the viability of the limbs. In these cases, sometimes an abrupt onset of intermittent claudication may be the first symptom.

(2) Transitory or pseudo-embolic type where the features to begin with are those of transitory aortic obstruction but recovery soon occurs with return of pulsations without any permanent ischaemic damage.

More than half of the cases reported by Read *et al.* (*loc. cit.*) lacked the classical picture and in them, particularly those of subacute type, the diagnosis was often made in retrospect.

Recent advances in the field of vascular surgery coupled with poor results with conservative medical treatment have prompted many surgeons to undertake embolectomy in such cases. Albright and Leonard (1950) recorded 26 cases with cure after successful embolectomy while Pool and Farrar (1952) reported the thirty third successful aortic embolectomy. Blum (1955) reported 6 cases with only one survival. Frank *et al.* (1956) while reviewing the literature on this subject could find only 43 successful, embolectomies till 1956. For surgery to be successful, giving gratifying results, it is imperative that it should be undertaken within the first few hours of its occurrence. Albright and Leonard (*loc. cit.*), Basu and Dass (*loc. cit.*) emphasise that lumbar sympathectomy in addition to embolectomy, should be seriously considered when the interval between embolism and the operation is more than six hours. Read *et al.* (*loc. cit.*), on the other hand, remark that the common belief that embolectomy is the only hope for these patients stems from frequent reports of surgical successes and conservative failures. Thiessen and Marscen (1952) could find only 3 survivals out of 34 successful embolectomies after 5 years and in fact 15 patients had died within a year. Read *et al.* (*loc. cit.*) state that there is no single treatment which can be considered the best for all cases and they recommend that active medical treatment of embolism should be started immediately because aortic embolectomy though it may be life- and limb-saving yet the end result is often disappointing.

Proper treatment of the underlying heart disease is of paramount importance in the management of such cases and particularly auricular fibrillation should be controlled without much delay. Arterial embolisation in mitral stenosis should be considered as an indication for valvotomy and if that is not possible the patient should be kept on long-term anticoagulant therapy.

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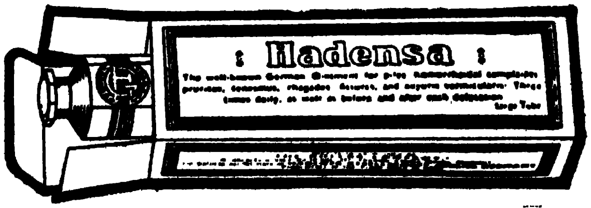

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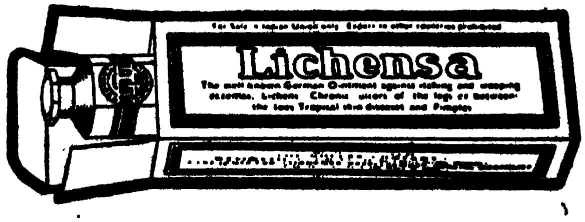

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The medical treatment consists of absolute rest to the affected limbs keeping them either at the same level or in slightly dependent position, and on no account should the limbs be elevated, sedatives and analgesics to relieve the pain and ensuring good sleep, anticoagulants for preventing the spread of thrombosis and vasodilator drugs for help in establishing the collateral circulation. This should be persisted if within a few hours there is some improvement as shown by return of power, sensation and warmth, otherwise embolectomy should be undertaken without much delay.

The case reported here presented a classical picture of acute catastrophic type of sadlle embolism at the aortic bifurcation occurring in a case of mitral stenosis, precipitated by the onset of auricular fibrillation where successful embolectomy was done followed by return of power, sensation and warmth in the legs but he suddenly expired due to a subsequent massive embolisation. As a matter of fact, it is the recurrence of these embolic phenomena which adversely affects the prognosis in such cases.

SUMMARY

A case of mitral stenosis with auricular fibrillation resulting in embolism at aortic bifurcation and treated by embolectomy is reported.

ACKNOWLEDGMENT

The author is very thankful to Dr. G. S. Sekhon for performing embolectomy in this case.

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TRICHOBEZOAR

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Trichobezoars have been reported off and on in the literature and perhaps less than 400 cases have been reported so far. The rarity of 'recurrent' trichobezoar has prompted the authors to report two cases in one of which the hair ball in the stomach recurred 3 years after the first one was removed.

CASE REPORTS

CASE 1 :

B.K., female child aged 5 years, was admitted in the V. J. Hospital, Amritsar, on 2-11-60 with the following history :

Three months prior to admission the child developed pain in abdomen, and the mother discovered a mass in the upper abdomen. A physician was consulted who treated her as a case of enlarged malarial spleen, but without benefit. Another physician advised repeated purgation which had no effect on the size of the mass ; but the child instead developed generalised oedema and progressive weakness. She was then referred to hospital for treatment.

On examination, the child looked very poorly nourished, with generalised oedema. A firm mobile intra-abdominal mass, 4″ × 2½″, was palpable in the epigastrium, extending to both the hypochondria. Liver and spleen were not palpable. On direct questioning, the mother admitted that the child had the habit of swallowing hair.

Investigations—Haemoglobin : 9·4 g. per cent Urine and stools showed nothing abnormal. Total leucocytic count 6500/c.mm., with polymorphs 37 per cent, lymphocytes 58 per cent, monocytes 1 per cent, eosinophils 4 per cent. A clinical diagnosis of trichobezoar was made and was confirmed on barium meal study of the stomach.

After combating anaemia and generalised oedema, the patient was operated upon on 12-12-60.

Operation (K. S. Kochhar)—Under general anaesthesia, the abdomen was entered through a left paramedian incision. Exploration revealed a firm mass filling the whole stomach. Gastrotomy was performed and a trichobezoar forming a complete cast of the stomach was removed. Gastrotomy wound was closed in two layers. Further exploration did not reveal any hair ball elsewhere in the gastro-intestinal tract. Laparotomy wound was closed in layers.

Postoperative period was uneventful.

Second admission—Three years later, on 4-10-1963, the patient then eight years old, was readmitted in the V. J. Hospital, Amritsar, with history of progressive weakness, generalised oedema, occasional vomiting and a mass in the upper abdomen. On examination, she was found moderately anaemic, with generalised oedema. Her height was 113 cm. and weight 16·5 Kg. Haemoglobin 9·0 g. per cent. Total leucocyte count 6800/c.mm., with polymorphs 56 per cent, lymphocytes 40 per cent, monocytes nil, and eosinophils 4 per cent. Mantoux test was negative. Urine and stools showed no abnormality.

On examination of the abdomen a 7 cm. left paramedian linear scar of previous operation was present. A firm mobile intra-abdominal mass, 5″ × 3″, was palpable in the upper abdomen extending to both the hypochondria. Liver and spleen were not palpable.

A clinical diagnosis of recurrent trichobezoar of the stomach was made. After correcting the nutritional deficiency, she was submitted to surgery on 19-12-63.

Operation (K. S. Kochhar)—The abdomen was entered through the old left paramedian scar. The peritoneal adhesions were separated. Gastrotomy was performed and a big trichobezoar filling the whole of stomach was removed. Gastrotomy wound was closed in two layers. Further exploration of the abdomen was negative. The laparotomy wound was closed.

Postoperative period was uneventful.

CASE 2

G.S., male child aged 12 years, was admitted in the V. J. Hospital, Amritsar, on 5-6-1963 with complaints of generalised oedema and a mass in the upper abdomen of 1½ months' duration. On interrogation, history of trichophagia was admitted by the patient ; but it was learnt he had stopped eating hair 3 years prior to admission in the hospital.

On examination, the patient was found moderately anaemic. There was well marked generalised oedema with free fluid in the peritoneal cavity. Heart and lungs were normal.

On palpation of the abdomen, a firm mobile mass, 5″ × 3½″, was found present in the epigastrium with the left extremity of the mass going under the left costal margin. Liver and spleen were not palpable. A clinical diagnosis of trichobezoar in the stomach was made.

Investigations—Haemoglobin 9·6 g. per cent. Total leucocyte count was 11200/c.mm. with polymorphs 70 per cent and lymphocytes 30 per cent. E.S.R. 4 mm./1st hour (Westergren). Urine was negative. Stools revealed ova of hookworm but no hair.

Plain x-ray abdomen showed a soft tissue mass in the epigastric region. Barium meal study showed extensive filling defect as seen in trichobezoar.

Treatment—The patient was dewormed and put on necessary corrective therapy to improve his nutritional status. He was discharged from the hospital on 8-7-63 with advice to report back after six weeks.

The patient was readmitted on 23-9-63 markedly improved in health. Generalised oedema had disappeared. Haemoglobin now was 12·2 g. per cent. Laparotomy was done on 10-10-63.

Operation (K. S. Kochhar)—Under general anaesthesia, the abdomen was entered through a left paramedian incision. Exploration revealed a big mass in the stomach. Gastrotomy was performed and a big trichobezoar forming a complete cast of the stomach, was removed. Gastrotomy wound was closed in two layers. Further abdominal exploration was negative. Laparotomy wound was closed in layers.

Postoperative course was uneventful.

DISCUSSION

A trichobezoar consists of a large quantity of swallowed hair firmly matted together in which are interspersed varying amounts of organic matter and decomposed food residue. Bigger hair balls form a perfect cast of the stomach. Hair balls are encountered mostly in young girls; but in the present cases, one was a boy aged 12 years and the other a young girl in whom the hair ball recurred three years after removal of the first one; obviously due to continued habit of trichophagia.

Occasionally cases have been reported where intestinal obstruction supervened due to migration of hair ball from the stomach to the small intestine.

Diagnosis of trichobezoar in the stomach can usually be made on clinical examination, provided the condition is kept in mind. The presence of a large, firm, mobile mass in the epigastrium, of the size and shape of the stomach is very suggestive, and the radiological appearances on barium meal study are characteristic.

SUMMARY

Two cases of trichobezoar are reported.

Both cases presented with generalised oedema, anaemia, progressive weakness and a mass in upper abdomen.

In the first case (B. K.) the hair ball recurred 3 years after the operative removal of the first one due to persistence of the habit of trichophagia.

ACKNOWLEDGMENTS

Our thanks are due to Dr. M. L. Aggarwal, Professor of Radiology, for necessary radiological investigations.

JOURNAL OF THE
INDIAN MEDICAL ASSOCIATION

CALCUTTA, OCTOBER 1, 1965

JOHN BURDON SANDERSON HALDANE

The late Professor J. B. S. Haldane was recognised as an eminent man of our time for more than one reason. He was a great scholar in a number of disciplines of the arts as well as of the sciences. A versatile genius, proficient in science, teaching, journalism and even politics, he dedicated his whole life in a deliberate and persistent effort to better the human society and to lift the common people up to the standards of the disciplines of modern science.

Prof. Haldane cherished, throughout his life, a deep sense of love for humanity and of respect for the established human values. His boyhood days of the late nineteenth and early twentieth century favoured the development of this mental make-up. Another very important factor that guided him in his boyhood days was the influence of his father—Prof. J. S. Haldane who was not only a pioneer physiologist of his time, but also one of the then revolutionaries in the field of physiology. The physiology of respiration got its first definite shape at the hands of this great scientist. But this is not all. He was also one of those few who actively participated in the popularisation of Claude Bernard's concept of *milieu interieur* among physiologists and thereby helped the emergence of a scientific "New Physiology" at the end of a long drawn mechanistic-vitalistic dispute[1]. The junior Haldane was in his teens then and was a close associate of his father whose affection and teaching had a lasting influence on his character. He cultivated a mental make-up that was affectionate towards his fellow-men, logical towards scientific problems, sacrificing towards the cause of science and, in the broader sense, towards the cause of humanity, bold and courageous towards the fulfilment of his own ideals and accepting towards new emergences. His interest for the biological sciences also came from the same source at the same time.

A biologist of wide reputation, he contributed to the subject both methodologically as well as experimentally. As regards methods he pioneered the extensive use of mathematics in biology with conviction because "Darwin thought in words. His successors today have to think in numbers"[2] and elaborately developed the statistical aspects of human genetics. As an experimenter, on the other hand, he was chiefly engaged in the study of genetics and enriched the subject considerably. His primary field of interest was, however, evolution the mathematical interpretation of which happened to be his chief concern in earlier days. It is in this field that he came across the beauty of genetical problems to which he afterwards shifted. Enunciation of Haldane's rule in 1922, determination of the condition for stable equilibrium of sex-linked genes, works on X-chromosome including the determination of its map distance, works on haemophiliacs, mathematical analysis of the effects of maternal-foetal incompatibility with the result to show that the presence of rhesus system remains associated with a state of unstable genetic equilibrium only. These are but a few of the successful contributions of Haldane to genetics. In biochemistry, his "one gene one enzyme" hypothesis was of much use both in fundamental as well as in clinical researches. These numerous contributions made him known as a great scientist throughout the world.

But let alone his scientific achievements which form a meagre part of the total Haldane. It is right that "I have been far too busy with my main occupations of research and teaching to evolve a complete philosophy of life"[3], but it is also true that he acquired the gifted vision of seeing the world simultaneously in her geological, zoological (with special reference to evolution), geographical, historical and sociological perspectives[4]. This rare type of consciousness, emanating from a fusion of several disciplines, gave rise to a concept of behaviour, characteristic of the man, that guided his life up to the end. As a result, now that he has departed and his complete life is present before us, we have, not a definitely "evolved" philosophy, but a set of events performed with courage in obedience to the established values, linked up with integrity and illustrative to his successors. His consciousness was always on guard against any perversion to this set of events by selfishness or any other agent.

The only identity of J. B. S. Haldane was therefore that he was nothing else than a common man gifted with consciousness. He came to the field of science just to satisfy his basic thirst for the knowledge of what happened in the past, i.e., of evolution. He loved mathematics since it can serve as a fine substitute for one's native intelligence where crude senses cannot work well. He was a teacher, a deliberate one indeed, who devoted himself to popularise science. His writings in this sphere clearly reveal that the author was in the mood of a common man who is telling his fellow-men what wonders he has seen in a place unknown to them so that they can decide together how to make a good use of those wonderful things. The only difference of Haldane with the common man was, however, that he was fully conscious about what he was doing; that is, he was completely in the know of the social consequences of a scientist's activity. Aware of the "Darwinism and its perversions"[5], he joined the political scientists to deplore the perversion of the doctrine of "the survival of the fittest" for serving as the basis of Hitlerism and warned biologists to see that this might not happen again in future.

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[1] HALDANE, J. S.—The New Physiology and Other Addresses, 1919, Charles Griffin and Company, London.

[2] HALDANE, J. B. S.—Everything Has a History, 1951, George Allen and Unwin Ltd., London, p. 219.

[3] *Idem*—The Inequality of Man and Other Essays, 1932, Chatto & Windus, London, p. vi (Preface).

[4] *Idem*—Everything Has a History, 1951, George Allen and Unwin Ltd., London.

He could also very easily anticipate the significance of the bulk of his contemporary neurophysiological researches by which "the great philosophical problems about knowledge and will are going to be pretty fully clared up"[6]. Nevertheless, he was not afraid of their sociological effects which might prove a big shock at the root of the established values. Instead, he liked to accept them with courage and complete resignation and thus showed the post-war twentieth century individual, bewildered by several agents like war, poverty and scientific analysis of values, an effective way out of the mesh. The same consciousness led him to be in constant battle against anything that threatens to kill the basic humanity. He could not go with the Communist Party in its attempt to distort science for the sake of a dogma ; nor could he tolerate the distortion of democracy that invited foreign troops to settle in England or the whims of a single man or a party causing the "mass murder" of the Port Said.

He did not like any egoism or prejudice. This is why he asked his Indian students not to groan for the unavailability of costly equipment ; but, instead, to make use of their native intelligence in research. He severely criticised the bureaucratic system and raised his voice against the inflated claims of the directors of many Indian research institutes to the authorship of each scientific paper coming out of those institutes. Many people might not have liked it ; but Haldane was aiming at a principle which the men at the helm of affairs of scientific research can ignore only to their detriment. He himself was really very inspiring to his junior collaborators. "Indeed, a sure way to annoy him was to attribute to him the work of one of his colleagues"[7].

Love of adventure was another basic human quality that found frequent expression in his character. Out of this, mixed with a spirit to sacrifice for the cause of science, he performed a good number of experiments on himself. Of these, his work on acidosis and on the physiological effects of high pressure and decompression on submarine crew, carried out with his wife, Dr. Helen Spurway, during World War II deserve special mention for the risk that was involved in them. Even the painful days of his last illness which proved fatal ultimately could not deter him from trying a drug on himself, as has been well documented in an article[8] elsewhere in this issue, just for the sake of advancement in cancer therapy. The detachment of the true scientific observer that he could bring to any problem is wonderfully typified in his last poem 'Cancer's a Funny Thing'[9], the opening lines of which are:

> "I wish I had the voice of Homer
> To sing of rectal carcinoma,
> Which kills a lot more chaps, in fact,
> Than were bumped off when Troy was sacked."

Even his death exemplified this consciousness. He forbade floral wreaths to be laid on his dead body and donated his dead body towards medical research.

Thus, Haldane's life illustrates the role of the conscious individual in the society. This is to live a simple life with the basic humanity revealed in all its instincts, intellects and activity intact. "It was a good show"[10] performed with the sportsman's awareness of the spectators without compromising his sincerity for the play. Everything was accepted with proper seriousness, but at the same time with a very easy attitude, undaunted even by his carcinoma. This attitude is befitting the age and a man of his calibre who had a mind to give a bold leadership to his fellow-men who were not adequately trained up in the order of the day. In doing so he made us remember of the fighting tradition of the progressing humanity at this moment of the "broken images". This is for what posterity owes him most.

ACHINTYA K. MUKHERJEE
ASHIS K. SINHA

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[5] *Idem—Ibid.*, p. 216.

[6] *Idem*—A Banned Broadcast and Other Essays, 1946, Chatto & Windus, London, p. 140.

[7] *This is Britain*—**5(24)** : 15, 1934.

[8] SANYAL, S. N.—*J. Indian M. A.*, **45** : 369, 1965.

[9] HALDANE, J. B. S.—*Your Health*, **13** : 304, 1964.

[10] *Idem*—The Inequality of Man and Other Essays, 1932, Chatto & Windus, London, p. 224.

CURRENT MEDICAL LITERATURE

Fluid Retention Produced by Guanethidine

SMITH, A. J. (*Circulation*, **31** : 491, 1965) from the Department of Therapeutics, Royal Infirmary, Sheffield, England, observed total exchangeable sodium and blood volume increase during the first year's treatment of seven hypertensive patients with guanethidine. Creatinine clearance values fell over the same period.

A similar change was seen in two patients receiving reserpine. It is suggested that the haemodynamic changes produced by hypotensive drugs are insufficient completely to explain the observations. A direct effect of guanethidine on sodium reabsorption in the kidney may also be involved.

Scintillation Scanning of the Liver

ACHAVAL, A., TAUXE, W. N. AND GAMBILL, E. E. (*Proc. Mayo Clin.*, **40** : 206, 1965) from Mayo Clinic, Rochester, Minn, reviewed their experience with scintillation scanning of the liver. This procedure involved minimal discomfort, risk, and radiation exposure, and it could be performed on very sick patients. No scans were falsely suggestive of space-occupying lesions, even in the presence of severe parenchymatous disease. The diagnosis of cirrhosis could be suspected from the characteristic pattern of the scan. Of the 36 scans performed on patients with space-occupying lesions, 23 were diagnostic and nine were suggestive of such lesions. The author believed that if hepatic scans were performed routinely before doing needle biopsies, the percentage of false-negative biopsies would be reduced. If there was no obvious impairment of hepatic function, nonvisualisation of the gallbladder was an indication for further studies of the biliary tract. The method produced scans that were reproducible and could be utilised to follow the evolution of tumours and their response to treatment.

Significance of the Lupus Erythematosus Cell Phenomenon in Older Women with Chronic Hepatic Disease

ALARCON-SEGOVIA, D., BARTHOLOMEW, L. G., CAIN, J. C. AND BAGGENSTOSS, A. H. (*Proc. Mayo Clin.*, **40** : 193, 1965) from Mayo Clinic, Rochester, Minn, observed chronic hepatic disease associated with the LE cell phenomenon in seven women more than 45 years of age. In these older women, systemic manifestations were less common than in younger women with the same syndrome previously reported from their institution. In four of the seven cases, liver biopsy revealed active hepatitis; in three of these, subsequent necropsy showed postnecrotic cirrhosis. The age distribution in chronic hepatic disease associated with the LE cell phenomenon is similar to that in systemic lupus erythematosus but different from that of postnecrotic cirrhosis in women. It is suggested that these are patients with either a lupus diathesis or overt systemic lupus erythematosus who develop viral hepatitis. The apparent subsequent rapid progression to postnecrotic cirrhosis may be mediated by autoimmune mechanisms.

The Syndrome of Dehydration, Coma and Severe Hyperglycaemia without Ketosis in Patients Convalescing from Burns

ROSENBERG, S. A., BRIEF, D. K., KINNEY, J. M., HERRERA, M. G., WILSON, R. E. AND MOORE, F. D. (*New Eng. J. Med.*, **272** : 931, 1965) from the departments of Surgery and Medicine, Harvard Medical School at the Peter Bent Brigham Hospital, described a case of the syndrome of glycosuria, dehydration, coma and severe hyperglycaemia without ketosis in the postburn period. The literature concerning this syndrome is discussed. It is postulated that this syndrome results from the failure of insulinogenic reserve of the pancreas, which in turn follows the prolonged feeding of diets high in carbohydrates. Though carbohydrate metabolism does proceed, and ketosis is thus averted, the glucose intake exceeds the amount that can be metabolised. Coma is secondary to the marked degree of hypertonicity present.

An awareness of this syndrome and its possible occurrence in any patient on prolonged feedings high in carbohydrates is needed if cases are to be recognised early and serious sequelae prevented.

Prevention is based on the avoidance of long continued intake of over 300 g. of carbohydrate per day.

Rheumatoid Lung Disease

PATTERSON, C. D., HARVILLE, W. E. AND PIERCE, J. A. (*Ann. Intern. Med.*, **62** : 685, 1965) from the Department of Medicine and Pathology, University of Arkansas Medical Center, Little Rock, Ark, reviewed over 700 patients with rheumatoid arthritis. The study revealed eight instances of moderate or severe diffuse pulmonary fibrosis. The course of the pulmonary disease was variable but characterised by dyspnoea on exertion, the frequent occurrence of subcutaneous nodules, clubbing of the fingers, and in three instances, cor pulmonale with death. There was no correlation between the severity of arthritis and the severity of the lung diseases. Histologic examination of the lung in one patient revealed a progression from diffuse interstitial pneumonitis to diffuse pulmonary fibrosis over a period of 5 years. It was concluded that the lung tissue in patients with rheumatoid disease is exceptionally reactive and that much of the pathology in the lung may be accounted for by an exceptional tissue response to ordinary pathogenic stimuli.

Dextran in the Treatment of Thrombophlebitis

COX, E. F., FLOTTE, C. T. AND BUXTON, R. W. (*Surgery*, **57** : 225, 1965) from the Departments of Surgery, University of Maryland School of Medicine and Maryland General Hospital, in their clinical trial demonstrated that dextran, when used early in the course of thromophlebitis appeared to be an effective treatment. In the dosage range used, there were no untoward reactions. The drug was easily administered, required minimal laboratory control, and avoided the potential hazards of conventional anticoagulant therapy. Work by many investigators has shown dextran to be effective in increasing capillary-bed flow. The authors' study supported this thesis. The exact mechanism by which dextran brings about these changes is unknown, but by increasing suspension stability of red cells, dextran may prevent sludging or thrombosis at the capillary level.

Evidence presented by chemical changes in the blood suggests that there is capillary-bed stasis ; the associated arterial spasm is well documented by the plethysmographic changes. These tests constitute the most clearly objective evidence available for confirming a clinical diagnosis of thrombophlebitis. There is no evidence available that dextran is a thrombolytic agent, and the data presented upon patients with thrombophlebitis of longer duration than 48 hours confirms this.

No attempt has been made in their study to compare dextran with other forms of therapy for thrombophlebitis. Further investigations will ultimately determine the role of this drug in thrombophlebitis.

Competence of the Tricuspid Valve in Pulmonary Heart Disease (Cor Pulmonale)

SHERMAN, W. T. AND FERRER, M. I. AND HARVEY, M. (*Circulation*, **31** : 517, 1965) from the Department of Medicine, Columbia University, College of Physicians and Surgeons, and the Cardiopulmonary Laboratory of the First Medical Division and the Chest Service, Columbia University Division, Bellevue Hospital, New York, reviewed seventy right atrial pressure curves obtained by cardiac catheterisation of patients with cor pulmonale. Only one right atrial tracing showed a regurgitant pressure wave, despite a wide distribution of right atrial mean, right ventricular end-diastolic, and pulmonary artery mean pressures, systemic blood flow, and despite the presence of peripheral venous congestion at the time of study in 46 per cent of the cases. This tricuspid regurgitation was probably due to the haemodynamic consequence of a prolonged P-R interval, an unusual finding in cor pulmonale. Hence it can be concluded that uncomplicated cor pulmonale rarely produced tricuspid regurgitation, as judged by the right atrial pressure curve.

The clinical signs often attributed to tricuspid regurgitation when noted in the presence of right ventricular failure are most probably explained by the sudden reversal of flow from atrium to veins, which is consequent to the large pressure variations originating in a congested right atrium.

Treatment of Heart-block with Long-acting Isoprenaline

BLUESTONE, R. AND HARRIS, A. (*Lancet*, **1** : 1299. 1965) from St. George's Hospital, London, write :

75 patients with symptoms due to heart-block were treated with a long-acting formulation of isoprenaline ('Saventrine') over a two-year period (average ten months).

Treatment was successful in 31 patients, who are now symptom-free ; and none have relapsed after an average of ten months. Artificial pacing was necessary in 32 patients, of whom 29 continued to have symptoms and 3 developed intolerable side effects from the drug, although their Stokes-Adams attacks were stopped.

Patients in sinus rhythm with intermittent heart-block were the most difficult to treat ; long-acting isoprenaline, in adequate dosage to prevent Stokes-Adams attacks when in block, tended to cause troublesome supraventricular tachycardias when in sinus rhythm.

In patients subject to ventricular tachycardia or fibrillation, long-acting isoprenaline can precipitate prolonged episodes of arrhythmia, and this was thought to have been the cause of death in 7 patients. Because of this risk, especially in patients prone to spontaneous episodes of ventricular arrhythmia, a period in hospital is essential, with electrocardiographic monitoring, while the patient is given sublingual or intravenous isoprenaline. In the absence of ventricular arrhythmias, oral administration may then be started.

Side effects were seen in 17 patients—principally sweating, tremor and palpitation—but it was possible to continue the treatment in all but 3.

Electrocardiographic Changes Associated with Subarachnoid Haemorrhage

HOFFBRAND, B. I. AND MORGAN, B. D. G. (*Lancet*, **1** : 844, 1965) from the University College Hospital, London, write :

A patient with subarachnoid haemorrhage displaying the characteristic E.C.G. changes developed acute pulmonary oedema. These E.C.G. abnormalities indicate potentially fatal impaired cardiac function. In the management of intracranial haemorrhage the routine recording of E.C.G. changes could save the lives of a small number of patients whose intracranial lesions are not lethal in their own right.

Pulmonary Hypertension due to Obstruction of the Intrapulmonary Veins

STOVIN, P. G. I. AND MITCHINSON, M. J. (*Thorax*, **20** : 106, 1965) from Papworth Hospital near Cambridge and the Department of Pathology, Cambridge University, report the case of a 41-year-old man who died from pulmonary hypertension. Lung biopsy in life and necropsy studies showed that the pulmonary hypertension was due to obstruction of the small and medium-sized pulmonary veins by organised thrombus and an oedematous intimal swelling. There was serological evidence of a coincidental toxoplasmic infection, the significance of which is discussed.

Dietary Protein and Renal Failure

MCCRACKEN, B. H., PEARL, M. A. AND CARVAJAL, E. (*New Engl. J. Med.*, **272** :1050, 1965) from the Department of Medicine, Tulane University School of Medicine write :

Patients with chronic renal failure were studied to determine the extent to which diets low in protein may supplement glucose feeding without appreciably increasing total protein breakdown and hence the degree of uraemia. A basic regimen of 100 g. of carbohydrate was supplemented by 3 eggs, 6 eggs, a diet containing 20 g. of protein and a diet containing 30 g. of protein. Protein catabolism was estimated by measurement of total daily urea production.

The results suggest that in these patients with low rate of protein catabolism, a diet containinn 20 g. of protein may be fed without increasing protein catabolism appreciably even when the diet contains mixed second-class rather than first-class protein. A diet containing 30 g. of protein does result in increased urea production, an increase that is only partially prevented by anabolic steroid therapy.

Treatment of Pyelonephritis

McCabe, W. R. and Jackson, G. G. (*New Engl. J. Med.*, **272**: 1037, 1965) from the Department of Medicine, Research and Educational Hospitals, University of Illinois College of Medicine, and the Research Laboratories, West Side Veterans Administration Hospital evaluated specific therapeutic regimens and laboratory studies in 252 patients with chronic pyelonephritis to define bacterial, host and antibiotic factors influencing treatment. Although bacteriuria was eliminated during the therapy in 80 per cent of the patients only 81, or one third, remained free of bacteriuria during the three-year period of post-treatment observation. Two distinct patterns of reappearance of bacteriuria that differed in their pathogenesis and relation to therapy were observed. Relapses with the original strain reflected true therapeutic failure, but reinfections with different bacterial species or serotypes appeared to result from increased susceptibility of successfully treated patients to new urinary-tract infections rather than treatment failure.

Causes for the majority of relapses could not be determined. Approximately 40 per cent resulted from bacterial resistance to the antimicrobial agent used and were probably preventable. The host factors studied—hypertension, renal insufficiency, structural abnormalities and mild obstructive uropathy—did not influence the frequency with which the infecting strain was eradicated but appeared to predispose to reinfection. Patients with these abnormalities acquired new infections at a rate twenty to forty times that of the general population, and studies of catheter-associated infections suggested that susceptibility to reinfection may partially result from an impaired capacity of the bladder to clear bacteria.

Comparison of the effectiveness of 7 antibiotic regimens demonstrated sulphonamides to be least effective, but no significant differences could be detected between other agents. The failure of combinations of antimicrobials to be more effective than a single agent resulted from antagonism between components of the antibiotic combinations demonstrable *in vivo*. Inhibitory antibiotic activity against the infecting organism in the urine during treatment was a pre-requisite for ensuring eradication of bacteriuria, but correlation between *in vitro* serum activity and eradication of bacteriuria was poor. Repeated courses of therapy after relapse or reinfection were as effective as the initial treatment course.

Clinical Features of Fluid Retention Complicating Treatment with Guanethidine

Smith, A. J. (*Circulation*, **31**: 485, 1965) from the Department of Therapeutics, Royal Infirmary, Sheffield, England, writes:

Forty-four (32·8 per cent) of 134 patients treated continuously with guanethidine for a period of at least 12 months developed recognisable fluid retention. Previous oedema may be a predisposing factor and fluid retention occurred more commonly in women. Neither of these factors offers a complete explanation of this side effect.

No evidence has been found to suggest that fluid retention occurs preferentially in patients with renal or cardiac insufficiency. The findings are compatible with a universal fluid retaining influence of guanethidine presenting as a graded phenomenon.

Fluid Retention Produced by Guanethidine

Smith, A. J. (*Circulation*, **31**: 490, 1965) from the Department of Therapeutics, Royal Infirmary, Sheffield, England, writes:

Total exchangeable sodium and blood volume increased during the first year's treatment of seven hypertensive patients with guanethidine. Creatinine clearance values fell over the same period. A similar change was seen in two patients receiving reserpine. It is suggested that the haemodynamic changes produced by hypotensive drugs are insufficient to completely explain the observations. A direct effect of guanethidine on sodium reabsorption in the kidney may also be involved.

Extension of Cervical Cancer to the Superficial Inguinal Lymph Nodes

Crichton, D. (*S. Afr. Obstet. Gynec.*, **3**: 23, 1965) from the Department of Gynaecology and Obstetrics, King Edward VIII Hospital and University of Natal, writes:

1. The frequency of spread of cervical cancer to the superficial inguinal lymph nodes was assessed in this study of 591 cases.
2. Malignant spread to the superficial inguinal lymph nodes did not occur when a clinical assessment of stage 1 spread had been made, but when the clinical staging was II or III the likelihood of spread rose to 5·1 and 5·2 per cent respectively. In stage IV growths the superficial inguinal lymph nodes were malignant in 14·1 per cent of cases.
3. The need to base the diagnosis upon the biopsy of the superficial inguinal lymph nodes, as opposed to a clinical appraisal, was proved by the discovery of an error rate of 30 per cent in clinical diagnosis when the lymph nodes were malignant and 13 per cent when they were benign.
4. Biopsy of the superficial inguinal lymph nodes did not predispose to subsequent malignant ulceration in the groin, even if the nodes were malignant at the time of biopsy.
5. The extent of spread of the carcinoma down the vagina favoured spread to the superficial inguinal lymph nodes, and similarly a 5-fold increased likelihood of involvement was encountered when there had been malignant invasion of the bladder.
6. The life expectancy of patients in whom cervical cancer has spread to the superficial inguinal lymph nodes is short.
7. The important recommendation which therefore stems from this study is that preliminary histological examination of superficial inguinal lymph nodes should be performed upon all patients whose carcinoma has spread much beyond the cervix before reaching a final decision to embark upon surgery for cervical cancer.

CURRENT TOPIC

V INTERNATIONAL THYROID CONFERENCE

A Report on the Proceedings

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The Fifth International Thyroid Conference was held this summer in Rome under the joint auspices of the International Group, the American Thyroid Association and the London Thyroid Club. About 400 delegates from different parts of the world attended.

The opening ceremony was performed with pompous fanfare in the Campidoglio in the presence of the Italian government representatives. The Scientific Sessions were held at the Cavalieri Hilton Hotel, 128 papers were presented while another 262 papers were read by title. There were eight main sessions which included presentation of the work on the biochemistry of thyroid gland and thyroidal iodoproteins, diagnostic tests, iodine kinetics, thyrotropic factors, thyroid cancer and metabolic and therapeutic aspects of thyroid disorders. Eight round table discussions were held on certain aspects of thyroid disorders of common interest. This included subjects such as radiobiology of the thyroid gland, thyroidal tumours and their treatment, neurohormonal control of thyroid function, clinical aspects and laboratory techniques for thyroid studies, endemic and congenital goitres, metabolic actions of thyroid hormone, immunological aspects of thyroid diseases, toxic and non-toxic goitres. In this report on the proceedings of the conference an attempt has been made to highlight the works presented at this international gathering.

ELECTRON MICROSCOPY

Electron microscopy of the normal thyroid gland had shown that the follicular cells had large regular spheroidal nuclei, moderate numbers of microvilli and numerous ribosomes both free and in association with the endoplasmic reticulum. The ergastoplasmic sacs contained two components, one granular and indistinguishable from colloid, and the other filamentous.

High resolution auto-radiography with electron microscope had been used to study the intracellular kinetics of radio-iodine and steps of thyroglobulin formation in the rat thyroid. Accumulation of radio-iodine seemed to occur in the follicular cells 6 hours after injection of 1 mc of I^{131}. Less of radio-iodine was concentrated by the apical vesicles, the ergastoplasmic sacs, droplets of the Golgi zone, and the interior of the nucleus. No accumulation occurred in the basal zone or in the vicinity of the blood capillaries, Lupulescu, A. and Petrovici, Al (Rumania). Radio-autographic studies also showed that iodination occurred in the colloid of the follicle lumen within a distance not exceeding 10-15 μ from the apical surface of the follicular cells. Thyroglobulin molecules just at the cell surface were subject to iodination and proteolysis most. The rate of turnover of thyroglobulin in the colloid appeared to decrease exponentially as the distance from the cell surface increased, Nadler, N. (Canada).

THYROID CELL METABOLISM

The metabolism of the thyroid cellular sub-fractions has been studied. Mitochondrial respiratory control ratios (R.C.R.) had been studied with the phosphate acceptor, succinate and other incubation media and also the Clark oxygen electrode. Thyrotoxic mitochondria have been found to have low R.C.R. with or without A.T.P. presumably because of an active A.T.P.-ase, De Groot, Lj, Dunn, A.D. (U.S.A.).

Attempts have been made to purify and study the specificity of messenger R.N.A. in the subcellular fraction of the sheep thyroid gland. Thyroid m R.N.A. preparations were heterogeneous when analysed by ultracentrifugation on a sucrose gradient. A broad peak with maximum around 16S was obtained. Leucine C^{14} incorporation per mg. R.N.A. and per mg. ribosomal proteins was of same order of magnitude as the best preparations of *E. coli* m R.N.A., Cartouzou, G., Mante, S. and Lissitzky, S. (France). Enzyme peroxidase was located in the mitochondria and microsomes. Enzyme preparations contain 40 per cent apoenzyme and 60 per cent intact holoenzyme. Iodine was oxidised by the peroxidase in the thyroid tissue before it was incorporated into tyrosyl residues and ultimately into the thyroid hormones, Alexander, N. M. (U.S.A.).

IODINE KINETICS

Studies on iodine metabolism had been carried on in different age groups indicating significantly higher renal iodine clearance and a low plasma inorganic iodide in the adolescents. The amount of iodine accumulated into the gland was in absolute values, however, the same. It was due to a corresponding increased thyroidal clearance rate, Malvanx, P., Ponchon, G., Beekers, C. and De-Visscher, M. (Belgium). On low iodine diet, hamsters developed colloid goitre with iodine content of the goitre being up to 10 times normal but the iodothyronine of less than 1 per cent of the total iodine. The thyroid radio-iodine after one hour uptake was less than 3 per cent inorganic, therefore, the fast turnover was related to the thyroid organic iodine.

The iodinated products of hydrolysis of isolated colloid cysts were similar to those found in the non-cystic hyperplastic portions of the same thyroids, Van Middlesworth, L. (U.S.A.). Balance studies of iodine have been done especially in regard to the intestinal absorption. In thyrotoxic patients, faecal iodine levels were significantly higher than those in the euthyroid group. In patients with untreated hypothyroidism, faecal iodine was low. It was surmised that faecal iodine was derived mainly from the endogenous thyroid hormone, Harrison, M. T., Harden, A. M. C. G. and Wayne, E. (U.K.).

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* Recipient of Wellcome Research Travel Grant

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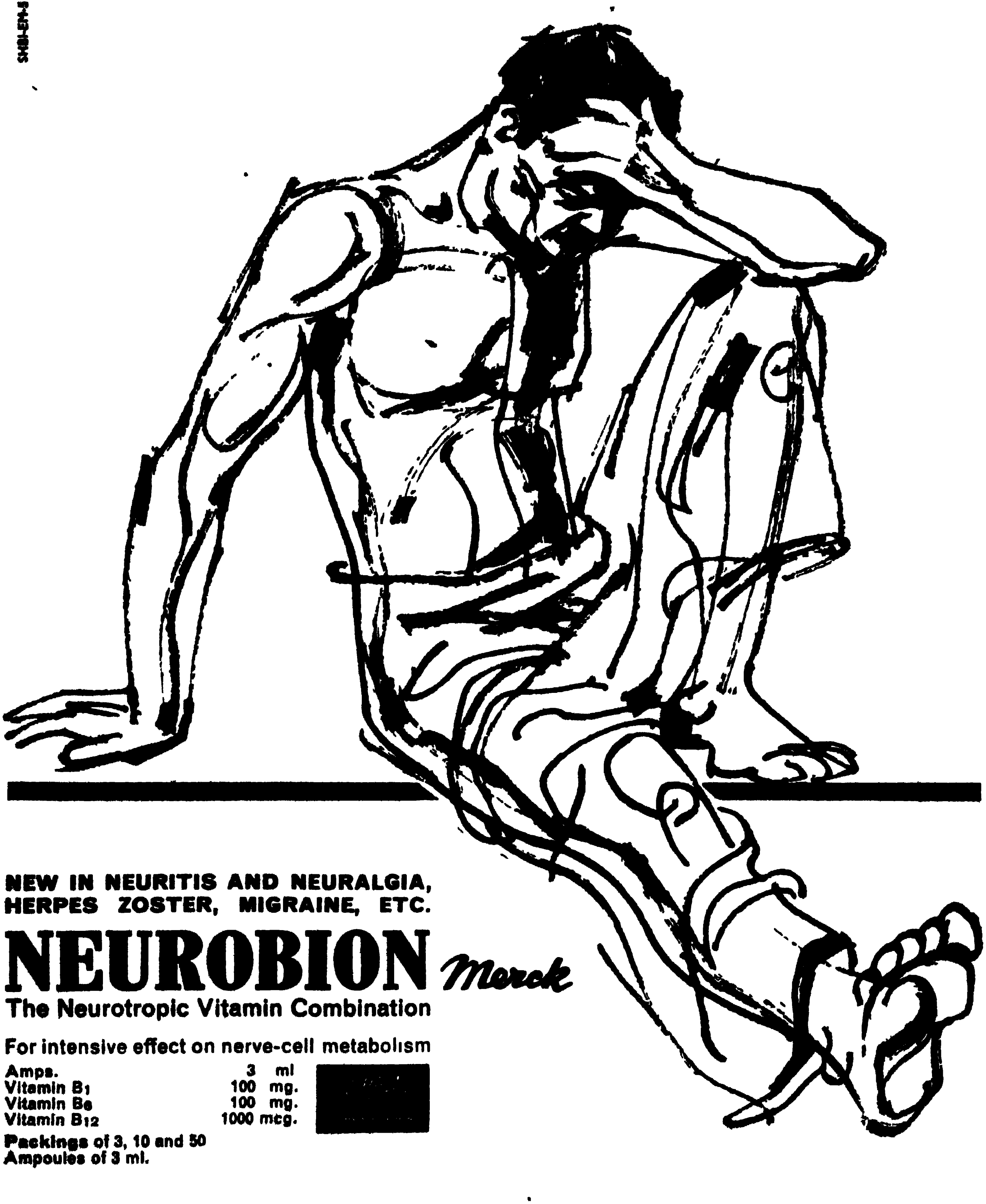

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THYROIDAL IODOPROTEINS

Thyroidal iodoproteins consist of 12S, 19S and 27S components on ultracentrifugation. This had also been shown on the pulse labelling experiments and sucrose gradient centrifugation. In lower vertebrates, the rate of iodination seemed to decrease and the iodine content to increase with the molecular size of the iodoproteins, Salvatore, G., Sena, L., Viscidi, E. and Salvatore, M., (Italy). Biosynthetic steps and the disaggregation of the various fractions had been the subject of studies by other investigators. There was evidence for presence of differences in the soluble and insoluble iodoproteins in the nodular areas (i.e., hot or cold) and the surrounding normal tissue.

The turnover of the iodine to thyroglobulin seemed accelerated in the hot nodules while in cold nodules the iodination of thyroglobulin was extremely reduced when compared to the non-nodular tissues and at times, thyroglobulin was not at all iodinated.

In the Van Meter Prize Essay by Oppenheimer, J. H. and Bernstein, G., (U.S.A.), the studies on the metabolism and physiological significance of thyroxine binding pre-albumin (T.B.P.A.) in man were presented. Immunologically pure T.B.P.A. was iodinated (I^{131}) for this purpose and mechanism responsible for T.B.P.A. depression in non-thyroidal illness and in the post-operative state studied. Increased fractional degradation and as well diminished synthesis were responsible for the lowered plasma concentrations. In acute injury, synthesis of T.B.P.A. was reduced. This resulted in a fall in the circulating thyroxine binding sites and so led to increased concentration of free thyroxine for the cellular metabolic needs. In chronic illness, there was a compensatory decrease in the total circulating thyroxine and so there would be a restoration towards normal of the free thyroxine concentration. The Dunhill memorial lecture was delivered by Wollman, S. H. (U.S.A.). He had studied the morphology and intrafollicular iodine kinetics as related to the hormone synthesis and secretion. Auto-radiographic evidence indicated that the membrane at the basal end of the cell was responsible for the concentration of radio-iodine by the follicle. One of the factors which caused its persistence at periphery was the content of dietary iodine. Resorption of colloid from the periphery of the lumen and its sequestration into droplets inwardly were the early steps in the secretion of the thyroid hormones.

Smaller follicles equilibrated radio-iodine faster. The protein bound iodine (P.B.I.) in the small follicles had a much higher specific activity than in the larger follicles. These evidences were taken to indicate the morphologic heterogeneity of the thyroid gland.

T.S.H.

Bakke, J. L. (U.S.A.) referred to the different methods for T.S.H. assay. There were about 12 different methods today utilising 8 different species. Though there was overall agreement in the results, the need for Human T.S.H. reference standard was stressed.

Utiger, R. D. (U.S.A.) described the radio-immunoassay method for human plasma thyrotropin (H.T.S.H.). H.T.S.H. activity was located in the 2-3S plasma protein fraction after G-200 filtration and could be virtually completely removed by absorption with antihuman serum. T.S.H. values were elevated in primary hypothyroidism. In untreated hyperthyroidism, values were undetectable in 25 out of the 34 patients studied. No activity was found in patients with spontaneous or surgical hypopituitarism or in most patients receiving exogenous thyroid therapy.

McKenzie, J. M. and Gordan, J. (Canada) referred to evidences for the Long-Acting Thyroid Stimulator (L.A.T.S.) to be a 7S gamma globulin and possibly that it is a product of the lymphoid tissues.

Dorrington, K. I., Carneiro, L. and Munro, D. S. (U.K.) felt that L.A.T.S. activity was an inherent property of specific (α2) globulin and may be an antibody.

Reduction of interchain disulphide bonds of active α2 globulin using a wide range of concentration of mercaptoethanol and alkylation of the resultant free sulphydryl groups did not affect the activity. Exposure to acid conditions prior to separation of the A and B peptide chains by gel filtration resulted in a striking loss of L.A.T.S. Thereafter the small amount of residual activity was confined to the A chain and remained long acting.

Limited proteolysis of active α2 preparation with papain under reducing conditions changed the response so that its time course resembled T.S.H. rather than L.A.T.S. Ion exchange chromatographic analysis of the digest showed that the short-acting thyroid stimulating activity was present in the S (Slow) fragment while the F (Fast) fragment was devoid of activity.

Although Dobyns, B. M., Rudd, A. and Wright, A. (U.S.A.) had surmised that L.A.T.S. and E.P.S. may be located in the same protein fraction, immunological data seemed to bring out the differences indicating L.A.T.S. and E.P.S. were not identical, Hennen, G., Winand, R. and Nizet, A. (Belgium).

Studies on the effects of T.S.H. on thyroid microsomal and cell metabolism revealed that T.S.H. stimulated D.P.N. Kinase reaction by which T.P.N. is formed from A.T.P. and D.P.N. Puromycin and actinomycin D did not inhibit this T.S.H. effect of new protein formation and R.N.A. synthesis. T.S.H. effect was, however, inhibited by substances which interfered with oxidative phosphorylation and A.T.P. generation, Field, J.B., Epstein, E. and Jarett, R. J. (U.S.A.).

Hall, R. (U.K.) presented experimental data to show that glucose and T.S.H. shared a common mechanism of action on nucleotide formation, that of increasing the supply of available ribose. T.S.H. mediated stimulation of glucose oxidation *via* the H.M.P. pathway could now explain four apparently diverse effects of the hormone on the thyroid, viz., nucleotide formation by providing ribose, iodotyrosine formation, degradation, and phospholipid biosynthesis by provision of N.A.D.P.H.

Taurg, O. A. and Thio, D. T. (U.S.A.) made attempts to study *in vivo* preparations to determine the action of T.S.H. on the protein synthesis and release of thyroxine from the thyroid gland. In rabbits, thyroidal preparations with intact blood supply were used for such experiments. No significant difference in response to T.S.H. was observed between saline infused and puromycine infused thyroids. It was concluded that the action of T.S.H. in releasing T_4 from the thyroid gland was independent of any effect on protein synthesis.

Becker, D. V. and Fourth, E. D. (U.S.A.) brought further evidence for persistence of hyperthyroid function in few instances after total surgical hypophysectomy. Role of T.S.H. in Grave's disease was thus doubted and postulation made that maintenance of thyroid hyperfunction in Grave's disease may be extra-pituitary in origin.

Racadot, J., Peillon, F., Sebaoun, J. and Gilbert, Dreyfus (France) noted regressive aspects of T.S.H. pituitary cells in cases of Grave's disease where L.A.T.S. had been detected in the serum. These facts suggested that thyrotoxic goiter may exist with regressive T.S.H. pituitary cells.

Development of Thyroid Function in Foetus

The human foetal thyroid becomes capable of concentrating iodine by the thirteenth week. Costa, A., Cottino, F., Delle Piane, M., Ferraris, G. M., Lenart, L., Margo, C., Patrito, G. and Zoppettic, G. (Italy) studied thyroid function and thyrotrophin activity in foetus at varying stages of development. No stable iodine was present in thyroid of a 7·8 cm. or 10-week foetus. The trapping function seemed to start by 12-13 week, 9·5 cm., foetus. Thyrotrophin activity was demonstrable both in the serum and in the pituitary homogenate of the foetus at this time.

Aboul Khair, S. A., Buchanan, T. J., Crook, J. and Turnbull, A. C. (U.K.) substantiated this work and in addition found support for this functional development by corroborative isotopic and histological studies.

Costa *et al.* (Italy) further showed that in the 14-week foetus, hormonogenesis was complete up to tri-iodothyronine and the M.I.T./D.I.T. and iodotyrosine/iodothyronine ratios were approximately equal to unity. In the foetus at term, serum P.B.I. was 60-70 per cent of that in the mother.

Endemic Goitre

In case of endemic goitre evidence seemed to be forthcoming for a number of host factors for the qualitative deviations of the hormonogenesis. It has been suggested that the environmental iodine deficiency only aggravated a genetically determined biochemical abnormality of the thyroid (Lewitus, Z. and Lubin, E., Israel).

Dynamics of iodine metabolism in a study carried out in Chilean Andes by Beckers, C., Barzelatto, J., Stevenson, C., Gianetti, A., Pardo, A., Bobaddila, P. and De Visscher, M. (Belgium and Chile) indicated that there was an efficient adaptation of the thyroid tissue to the plasma inorganic iodine level in the case of diffuse goitre, with evidence of partial failure in the multinodular goitre.

It had been speculated by these authors that chronic stimulation of thyroid could possibly lead to some intrathyroidal disturbances in hormone synthesis.

Ekpechi, O. L., Dimitriadou, A. and Russell Fraser, T. (U.K.) had evidence to show that the unfermented cassava eaten sparingly by the inhabitants of certain areas of Nigeria had goitrogenic effect. Cossava contained an antithyroid substance which acted like the thionomide goitrogen.

In reference to endemic goitre in Finland, Peltola, P. referred to the role of iodine deficiency to be questionable. He demonstrated that the cows consuming the goitrogen 1-5 Vinyl 2 thio-oxazolidone (V.T.O.) through the cruciferous weed, common in this area excreted this in their milk. Daily consumption of 100 μg of V.T.O. which would be present in 1 litre of milk and resulted in thyroid enlargement in 6 weeks.

Hetzel, *et al.,* (South Australia) commented on the success in treatment of endemic goitre following iodised oil administration which was given in injectable form once a year. The goitre rate was significantly reduced. Sooch, S. S. and Ramalingaswami, V. (India) reported the results of iodine prophylaxis by iodised salt and potassium iodate, the latter being a far more stable salt. The goitre in the age group less than 15 had declined considerably. No difference had been noted, in results when either preparation of iodine was used in two different endemic areas.

Nodular Goitre

The evolution of the adenomatous goitre, the nature of the iodoproteins and the management were discussed by Vague *et al.* (France), Loho *et al.* (Brazil), Horst (Switzerland), Salalie, G. B. *et al.* (Italy) and Medeirois Neto, N. G. (Brazil). It was considered likely that a 'Warm' nodule may be pituitary dependent, however, as indicated by the tri-iodothyronine suppression test, a relative independence from T.S.H. was seen in certain instances.

Toxic or autonomous adenomas were the cause of thyrotoxicosis in one third of all cases seen at Hamburg and Zurich. The scintigraphically proven suppression of radio-iodine uptake within the normal parenchyma after T_3 administration was considered typical for the compensated toxic adenomas, while the finding of a normal thyroid configuration with a hot nodule within it after exogenous T.S.H. identified the decompensated autonomous adenoma. These tests perhaps allowed differentiation against inborn abnormalities of thyroid figure, against nodular hyperplasia and the non-autonomous adenoma with increased iodine turnover.

Radiochromatography of serum and urine demonstrated quantitative but no qualitative difference between Grave's disease and toxic adenoma.

Selective destruction of toxic adenoma with radioiodine 25-30,000 rad, the normal thyroid parenchyma being protected by prior administration of T_3 or surgical enucleation of the adenoma, not resecting the normal parenchyma and avoiding ligatures of the thyroidal arteries were the methods of choice advocated in order of preference for the treatment of this condition. Following such procedures incidence of myxoedema was reduced too.

Adrenal Thyroid Relationships

Kinetic response to methopyrapone and dexamethasone was studied in the hyperthyroid patients by Ceresa, F., Angeli, A. and Strumia, A. (Italy) in an attempt to study the alterations in adrenocorticotrophin system in this situation.

Urine flow of the 17-O.H.C.S., μg./min. was measured, there was a lack of a significant increase in the total 24 hr. 17-O.H.C.S. excretion in hyperthyroid subjects indicating an inadequate adrenal inhibition of 11-β hydroxylase by methopyrapone or a partial refractoriness of the A.C.T.H. system. Responsiveness to dexamethasone inhibition was greater in hyperthyroid than in normal subjects. There was an increased rate of dexamethasone disappearance from plasma in such hyperthyroid patients. Tako, J. and Rado, J. P. (Hungary) studied alterations of the adrenocorticotrophin activity in response to anti-thyroid therapy. There was an increase of adrenocortical function while decrease of the functional adrenocortical reserve capacity in hyperthyroidism. During effective antithyroid therapy the functional reserve capacity of the hypophysis increased.

THERAPY WITH RADIO-IODINE

Smith, R. M. and Wilson, G. M. (England) encountered incidence of 30 per cent of hypothyroidism following treatment of hyperthyroidism with RI^{131} in years 1950-51 and this seemed to be still further rising.

Since 1960, a trial with 3 different doses was being conducted, 14,000 rads (given up after 3 years because of very high initial incidence of hypothyroidism), 7,000 rads and 3,500 rads. It would seem that with the smaller dosage, incidence of myxoedema was lower. There was only a negligible rise over the last 3-year period. However, the percentage requiring treatment with additional anti-thyroid drugs was large. There was no reported increase in incidence of carcinoma in those treated with antithyroid drugs and radiation as noted experimentally in the mice. Myhill, J. A., Hales, J. B. and Reeve, T. S. (Australia) reported on yet another formula based on the thyroid clearance rate, goitre size, age and sex to calculate the therapy dosage of RI^{131}. Those remaining euthyroid had average dosage of 13,400 rads while with the average radiation dose of 25,000 rads, 10 per cent were hypothyroid in 1-4 years following therapy.

THYROID AUTO-IMMUNITY

In the 300 sera tested, the serological tests as T.R.C., C.F.T., S.F.T. were positive in conditions other than chronic thyroiditis but the titres were generally low. Percutaneous thyroid biopsies were scrutinised in 103 instances. The sporadic non-toxic goitres showed evidence of focal thyroiditis up to 10 per cent and titres were not significant, Ahuja, M. M. S. (India), Andreani, D., De Santis, Di Matteo, Cassano, C. (Italy) and MaChoney, Mayo Clinic (U.S.A.) also presented data on similar lines. Doniach, D. (U.K.) had shown the great value of immunofluorescent techniques in studies of patients with thyroiditis.

Approximately 30 per cent of patients with chronic thyroiditis or thyrotoxicosis had gastric parietal cell antibodies in the serum and this was associated with hypochlorhydria or complete achlorhydria. 3 per cent of the 134 thyroid patients had antibody to intrinsic factor in the serum and this antibody showed a high correlation with achlorhydria and malabsorption of oral vitamin B$_{12}$, Irvine, W. J., Davies, S. H. and Sumerling, M. D. (Scotland).

The immunological response to thyroid damage following radio-iodine therapy for thyrotoxicosis was studied by workers at Edinburgh, Stockholm as well as those at Manchester. Though the former two groups noted a transient rise of the microsomal antibody, the latter group did not support this and any way felt that it could not be contributory for the high incidence of post-irradiation myxoedema now being observed.

THYROID CARCINOMA

Winship's study of 800 children with thyroid carcinomas showed that 77 per cent had received therapeutic radiation at some time during infancy and childhood. Doniach (U.K.) worked on the genesis of thyroid cancer and radiation both external and internal for induction of cancer in rats. Taylor, S. (U.K.) studied the effect of low iodine diet on induction of thyroid cancer in rats by irradiation. The incidence of tumour formation was inversely proportional to the dosage of external radiation used.

Money, W. L. and Rawson, R. W. (U.S.A.) produced 100 per cent thyroid tumours in a strain of rat on prolonged treatment with thiouracil. This was shown to be transplantable successfully only into a neonatally thymectomised host and following this procedure, the tumour, would grow readily when transplanted further into intact animals.

Cancerogenetic process of thyroid had been studied by electron microscope and histochemical means by Milcu, S. M. and Petrea, L. (Rumania). The cytoplasm and ergastoplasm in the cell undergo reduction and the mitochondrial alterations take place. Total nuleal acids are increased in thyroid tumours. Differences in the ultrastructure were reported in instances of various types of carcinoma of the thyroid such as papillary, follicular and giant cell carcinoma (Inman, D., Newman, R., U.K.). Autocytoradiography showed a progressive diminution of I^{131} incorporation and transfer in tumoural thyroid cells. The histological sections of portions of 2,114 thyroid glands from patients suffering from hyperthyroidism were studied for evidence of cancer at the Armed Forces Institute of Pathology, Washington, U.S.A. by Olen, E. and Kline, K. G. H. and the incidence of cancer was found to be 2·5 per cent. Only a few of these tumours had been suspected clinically. Most of the thyroid cancers were small and more than one half were of the occult sclerosing type, i.e., less than 1 cm. in diameter. These concomitant carcinomata were approximately in 4 : 1 ratio amongst the diffuse and the nodular toxic goitres.

CHROMOSOMAL STUDIES

High titres of thyroid auto-antibodies were reported by Fellinger, K., Hofer, R., Rothen Buchner, G., Schatz, H. and Schober, B. (Austria) in the sera of patients with gonosomal and autosomal aberrations. Alterations of secondary constrictions and morphological differences within the homologous pairs were noted in the chromosomal analysis from peripheral leucocytes of patients with Hashimoto's disease.

Al Saadi, A. A. and Beierwalte's, W. H. (U.S.A.) studied chromosomal changes in the thyroid cells during iodine depletion and repletion. At 29-40 days of iodine deficiency in inbred Fischer rats, 10-30 per cent of the thyroid cells had non-modal counts, ranging from 37 to tetraploidy. With further prolongation of iodine deficiency, hypodiploidy was the rule. On repletion the non-modal counts decreased. Studies on the thyroid gland of 13 human had been made in this manner.

Socially, grand receptions at Campidoglio, Palazzo Barberini and Castel S. Angelo gave a proof of Italian hospitality. Audience with His Holiness Pope Paul VI for the delegates brought the stay in 'La Citta Eterna' to its greatest heights.

NOTES AND NEWS

National Scheme for Cholera Eradication

The Government of India proposes to undertake a National Eradication Scheme for Cholera throughout the country during the Fourth-Plan period.

To make the cholera eradication scheme a success the Government has adopted a programme for adequate supply of drinking water throughout the country. A large number of tube wells will be sunk in areas where cholera breaks out in an epidemic form. The question of disposal of garbage and sewage will also be tackled on a priority basis.

According to the Central Health Department, 1967-68 is likely to be a year of cholera epidemic. The West Bengal State Government feels, however, that 1966-67 may be the epidemic year in West Bengal. Accordingly, the districts have been alerted by the State Government to prepare themselves for the outbreak of a virulent type of cholera in May-June next. The dictricts of Purulia, Bankura, Murshidabad, Burdwan and Midnapore in West Bengal are already faced with an outbreak of cholera. But excepting Purulia, cholera has broken out in the other four districts in a sporadic form.

West Bengal proposes to carry on the National Eradication Scheme on cholera during the first two years in the Calcutta Metropolitan Planning Organisation areas covering 34 municipalities, and in the districts of 24-Parganas, Howrah and Midnapore where cholera cases occurred almost regularly, every year.

Restriction on Use of X-ray Films

The Centre has suggested to the State medical authorities that instructions should be issued to conserve supplies of x-ray films and to restrict their use only in essential cases. The measure has been suggested as a result of recent import restricttions.

30 More Medical Colleges under 4th Plan

Thirty medical colleges will be opened throughout India during the Fourth Plan, Dr. K. N. Rao, Director-General of Health Services, recently announced at Madras.

Dr. Rao said that in view of the great demand for admission to medical colleges, the Government proposed to increase the number of seats in medical colleges during the Fourth Plan to 20,000 from the present 11,000.

He also disclosed that the Jawaharlal Institute of Postgraduate Medical Education and Research at Pondicherry would be run with French collaboration and there would be exchange of professors and students for study and research. The Institute would, in the long run, grow into a medical university for this region.

From Weaklings to Superboys

According to a report in *Sunday Mirror*, British Scientists are turning undersize weaklings into superboys in 100 days with hormone injections.

The hormone, chorionic gonadotrophin, was given to 53 physically immature boys. It made them taller, heavier, tougher and more confident, the paper said.

A 13-year-old gained 1½ inches in height, a stone in weight and became more muscular, while the injections also boosted the boy's mental outlook.

The hormone trials were carried out by Dr. Alec Coppen, of the Medical Research Council's neuro-psychiatric unit.

Radiation Survey to be Undertaken

A pre-operational survey laboratory has been commissioned at Tarapur by the Health Physics Division of the Atomic Energy Establishment, Trombay (Bombay), according to a report published in "Nuclear India", the establishment's monthly.

The laboratory, located near the site of the Tarapur Atomic Power Station, is designed to carry out radiation safety monitoring of the site and environment as part of the health physics programme.

To establish base line data for future reference the laboratory has initiated an active environmental monitoring programme to obtain information on population and cattle distribution, dietary and local habits of people, food production from land and marine sources, nature of soil, ground water movement and natural as well as artificial radioacitivity content in soil, air, sea, rain and drinking water.

Shortcut to Learning

A group of scientists led by Dr. Allan Jacobson, Assistant Professor of Psychology at the University of California, recently opened up the possibility of transferring whole memories from one person to another by means of injections.

Their experiments conducted on rats—showed that it might be possible one day to use the same method as a dramatic shortcut to learning for humans. They trained some rats to carry out specific tasks. Then they injected molecules from them into untrained rats.

The substance injected was a molelcule basic to life, ribonucleic acid (RNA). Dr. Jacobson said his results showed that the RNA molecule might encode memory in a somewhat similar manner as its cousin molecule. Deoxyribonucleic acid (DNA) encodes genetic information which produces the hereditary effects in living creatures.

Laughing Death

About half of the 8,000 women and girls living in New Guinea's eastern highlands seem certain to die from a mysterious disease known as laughing death, according to Sir Macfarland Burnet, Chairman of the

Papua and New Guinea Medical Research Advisory Committee.

The disease is officially called Kuru and Sir Macfarland has been closely connected with research into its cause. It generally attacks only females. Thousands have died from it.

The disease affects part of the brain, resulting in loss of muscular control and in incoordinated jerky movements. Death usually occurs within six months to a year.

It is sometimes known as the laughing death because lack of facial control gives the victim the appearance of constantly laughing. Sir Macfarland has described Kuru as the outstanding unsolved problem of medicine.

Health in India : Report at the World Health Assembly

The general mortality rate per 1000 population fell from 27·4 in the period 1941-50 to 16·3 in 1961-62, and the infant mortality rate from 182·5 to 109·7 per 1000 live births. In addition, the expectation of life at birth was raised from 32 to 49 years. Nearly 80 per cent of the country is now in either the consolidation or the maintenance phase of malaria eradication. The overall coverage in the smallpox eradication campign is about 70 per cent. By the end of 1966 the number of trained doctors available is expected to be between 85,000 and 86,000 giving the country a doctor/patient ratio of about 1 to 5800. By that time, too, the number of medical colleges is expected to reach a total of 82, with an annual admission capacity of 11,000 students. The population of India is increasing at the rate of nearly 10 million a year.

School Health Council's Recommendation

Extension of the mid-day meal programme to all schools, immunisation of at least 75 per cent of school children against communicable diseases, the removal and correction of remediable defects by providing facilities for medical examination at the primary and secondary school level and provision of hygienic surroundings in schools, are among the major items included in the minimum School Health Programme recommended by the National School Health Council at its third meeting held at Delhi.

The Council urged the Union Government to find funds to implement the minimum programme.

Overhaul of Haffkine Institute Suggested

A thorough reorganisation of the Haffkine Institute in Bombay has been suggested by the Committee appointed by the Government of Maharashtra to inquire into its working.

The Committee appointed by the Government in April last year, made a critical study of the existing facilities for research and manufacture of sera, vaccines and pharmaceutical formulations, its main functions.

A section of the Institute was engaged in evolving process for acquiring "patents". The subjects chosen for such processes, it was found, had not been well thought out or pre-planned. Often they were found to conflict with the processes already patented by foreign manufacturers, and therefore, could not be commercially exploited.

The Committee has suggested that the research and manufacturing activity should be bifurcated and separate staff allotted for them.

Other recommendations of the Committee are that a major portion of the manufacture of the biologicals, such as vaccines and sera should be carried out at Pimpri, and these departments should be shifted to that place. Their research counterpart may be retained at the Haffkine Institute.

The manufacture of non-biologicals, such as vitamin tablets and insecticides, should be done by a separate department, preferably placed under the Directorate of Public Health. A quality control department should be set up, to keep a vigilant eye on the quality of the products of the Institute.

Research in Rehabilitation of Heart Patients

Bombay's K.E.M. Hospital will begin shortly research in the rehabilitation of heart patients. The study will cover the patients' medical, psychological, social and vocational aspects. Using modern methods of investigation, the project also will attempt to evaluate the response of the heart and blood vessels to exercise, emotion and other factors.

The proposed four-year research project, the first to be undertaken in India, will be financed by a grant of Rs. 570,853 from the Vocational Rehabilitation Administration (VRA) of the United States Department of Health, Education and Welfare.

The money will help to obtain modern equipment and additional research staff for the hospital's department of cardiology.

Dr. K. K. Datey, Cardiologist at the K.E.M. Hospital will direct the project. Associated with Dr. Datey will be Mrs. Kamala Nimbkar, honorary consultant in occupational therapy at the hospital.

Toxicology Centre at Lucknow

The Co-ordinating Committee of the Ministry of Health and the Council of Scientific and Industrial Research has recommended to the Government the setting up of an Industrial Toxicology Centre at the Central Drug Research Institute, Lucknow.

The Committee felt that an Industrial Toxicology Centre was essential as industries were growing and industrial workers were more and more subjected to health hazards because of industrial poisons.

The Committee also felt that drugs were very costly in India and recommended that a panel of experts be set up to investigate the causes of the high prices.

Another important recommendation of the Committee was that a programme to attain self-sufficiency in the manufacture of medical instruments and equipment should be undertaken.

Condensed Licentiate Medical Course in Andhra Pradesh

The Medical Council of India has recently decided in principle in favour of the starting of condensed licentiate course for the holders of diplomas of integrated medicine granted by several States in the country.

According to a statement by Mr. Y. Sivarama Prasad, Minister for Health, Andhra Pradesh the Director of Medical Services, Andhra Pradesh Government, has already submitted proposals for the starting of D.M. and S. course at Gandhi Medical College, Guntur Medical College and Kurnool Medical College. The President of the Medical Council of India recently visited these institutions. He suggested that the course might be started in the three colleges mentioned and the duration of the course should be two years. Fifty students would be admitted in each centre and the course would be continued for five years so as to enable all the students to have the benefit of this shortened course.

The Medical Council had earlier stipulated that the licentiate course should be available to only those who had begun their integrated diploma course before 1960 and to those who possessed an integrated diploma recognised by the State Government for which a pass in S.S.L.C. or equivalent examination was the minimum qualification. The licentiate course would be open to those who had put in a minimum of two years for the study of modern medicine subjects in the integrated course.

The Minister further disclosed in course of his statement that the G.C.I.M. diploma-holders were at-present required to serve as house surgeons for one year in any district headquarters hospital and the question whether in addition to this, the student would have to be required to serve a period of apprenticeship at the end of the proposed course would be considered by the Government in consultation with the Medical Council along with the other question as to whither G.C.I.M. diploma holders without house surgeoncy could be admitted to the proposed D.M. and S. Course.

Non-barbiturates : Addiction Risks

The person who takes sedative drugs in abusive fashion may become addicted to them, whether the drugs are barbiturates or some of the newer non-barbiturates.

Carl F. Essig, M.D., chief of the section on Experimental Neurology, Addiction Research Centre of the National Institute of Mental Health, Lexington, Kentucky, speaking at a Symposium on Non-Narcotic Addiction at the 114th annual convention of the American Medical Association, said that seven of the newer non-barbiturate-sedative-hypnotic drugs had been reported to cause barbiturate-like intoxication and physical dependence (addiction).

The seven drugs were meprobamate, glutethimide, ethchlorvynol, ethinamate, methyprylon, chlordiazepoxide and diazepam, he said.

Excessive use of one or more of these sedatives could cause drowsiness, difficulty in thinking and incoordination of movement, continued Dr. Essig. The signs of intoxication were similar to those induced by barbiturates or alcohol. Also, in the same way as could alcohol or barbiturate intoxication, non-barbiturate sedative intoxication might contribute to traffic accidents, injury by falling, interference with work and violent or assaultive behaviour.

If a patient had become physically dependent upon a non-barbiturate sedative, abrupt withdrawal might result in a serious abstinence syndrome, Dr. Essig warned.

Typical minor symptoms of withdrawal were anxiety, tremulousness, muscle twitches, loss of appetite, weakness and insomnia. Major symptoms were generalised convulsions, sometimes with delirium and psychotic manifestations such as disorientation, delusions and hallucinations.

Dr. Essig said that death had been attributed to withdrawal of meprobamate and methyprylon.

Treatment of non-barbiturate sedative addiction required admission to hospital. Dr. Essig recommended substitution of barbiturates for the non-barbiturate drug, followed by gradual withdrawal of the substitute drug.

—*Medical News.*

CORRESPONDENCE

The Editor is not responsible for the views expressed by Correspondents

Research in Medical Science

SIR,—Research scientists in medicine occupy a very important position among scientists today, and it is heartening to note that the Government of India has decided to constitute a cadre of such workers to promote researches in medical science. The achievements of medical science have caught popular imagination to a degree that has never been seen before. It is, therefore, important to select and train research scholars who are capable of working as independent and creative investigators in their own right. The most important and complex instrument employed in research is the man himself, and future of research in medicine will depend upon the selection, care and preservation of research talents. The appointment to this cadre should be reserved for those who are distinguished in scholarship and have displayed both initiative and originality which are the hallmarks of research scientists. It is hoped that the cadre of research workers will be of a kind in which our gifted young men would pursue their work without any hindrance or limitations whatsoever. If this is granted, the rewards to this country will be rich indeed. For I believe that we do possess in this country not only enough talent to work for the advancement of human welfare, but also men and women, who, if left to their dedicated ends, can offer us greater knowledge which would make our life worth living in this planet. The success of the scheme depends on proper recruitment and support to the future generation of research scientists.

I am, etc.

Vellore T. M. KUMARASWAMI
5-5-65

Headache

SIR,—I have read with keen interest the article entitled 'Headache' published recently in *J.I..M.A.* (**44**: 588, 1965). Though otherwise it is an excellent article, I feel that there are some lacunae which should be filled in. Below I am mentioning some of them.

1. It should be mentioned that the pathway for psychological headache is through the autonomic nervous system. This nerve plexus enters the brain along with the carotid artery.

2. Classification of headache:

(a) Under the cranial neuralgias, the authors should have added supraorbital, auriculotemporal, posterior auricular and greater occipital neuralgias.

(b) Under headache arising from intracranial structures, they should have mentioned encephalitis and syphilis.

(c) Unfortunately, they have altogether omitted headaches of toxic origin, both exogenous and endogenous. These are:

(i) *Endogenous*—gastrointestinal, uraemic, bilious liver, gout, intestinal toxaemias, eclampsia, etc.
(ii) *Exogenous*—foul gas, poisonous gas, alcohol, tobacco, lead poisoning, toxic action of quinine, iron, salicylate.

(d) Traumatic headache (organic and functional) and

(e) Cough headache.

Under clinical picture, the timing of headache of different types has not been discussed. This is a very significant diagnostic feature, such as (i) heavy headache on rising in the morning is usually of uraemic origin; (ii) headache increasing with the rising of the sun is usually observed in cases of nasal sinusitis; (iii) recurrent nocturnal headache, specially coming at late hours of night, are usually observed in intracranial space-occupying lesions; (iv) sudden severe headache, coming periodically breaking the night's sleep is very often seen in histamine cephalgia; (v) evening headache after the day's work is very often due to eye strain or mental overwork; (vi) evening headache after a hearty meal is usually of hypertensive origin.

The mechanism of headache can broadly be discussed under two heads, viz., somatological and psychological.

1. Somatological:

(a) Muscular factor—In headache, there is very often sustained contraction and spasm of the muscles (skeletal) of head and neck.

(b) Vascular—There is initial vasoconstriction of the cerebral arteries, followed by dilatation and distension. Vasodilatation and cerebral vasopasm cause cephalgia.

(c) Humoral—There is transudation of fluid surrounding the blood vessels. This fluid lowers the pain threshold. The chemicals responsible for this condition may be serotonin and/or bradykinase.

2. Psychological:

Psychological headache is of varied origin. The different organs, parts of the body have different psychological values assigned to them by human beings. Psychologically, the head occupies a very high value, that is why after any head trauma the subject very often develops a very intractable headache which very often resists effective therapy. Headache is often a symbolic expression of some inner conflict, a dependency need, inner anxiety or depression. It may be a hysteric conversion symptom, the so-called clavus hystericus which gives rise to a boring pain in the vertex of the head. Headache not responding to any treatment may also be of schizophrenic origin.

Under 'treatment', the authors have omitted the most obvious, i.e., the routine treatment of headache with some palliative analgesic such as aspirin and coal tar derivatives, or with any of the proprietary preparations. Addition of codeine preparation is supposed to be very effctive in all the varied types of headache of somatogenic origin. Recently zactirin has been added to the list.

Cerebral arteries can be very effectively treated with corticosteroids, starting with 150 mg. twice daily, and rising to a maximum of 200 mg. twice daily for one month and then gradually tailing off to a maintenance dose which is continued for 3 to 9 months.

Under migraine a trial should be made with stemetil. Further, patients sensitive to ergot should get octinum or neo-octinum. As a last resort oxygen inhalation should be given a chance.

In muscle contraction headache, various meprobamate preparations such as chlordiazepoxide (librium) should be treated.

Psychogenic headaches may be treated with the newer tranquillising drugs such as chlorpromazine (largactil), meprobamate (equanil), anatensol, etc., failing which the patients should be referred to a psychiatrist.

In trigeminal neuralgia, the time honoured prescription with potassium bromide grains 10, tincture gelsemium minims 10, phenazone grains 7½ and aqua up to ounce ½, one dose t.d.s., should be tried.

I am, etc.

Dept. of Neurology &
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ARUN K. ROY CHOWDHURY,
M.SC., M.D.

REVIEW

Absorption and Distribution of Drugs—Edited by T. B. Binns, 1964, E. & S. Livingstone, Ltd., Edinburgh and London; 13·8 cm. x 21·5 cm., pp. 270; 37s. 6d.

This small but compact volume is based on a Symposium on Absorption and Distribution of Drugs held in London in 1963 under the auspices of the Association of Medical Advisers in the Pharmaceutical Industries (A.M.A.P.I.). The volume consists of 17 lucid and masterly papers covering 270 pages of which over a third is from the eminent worker, Dr. Bernard B. Brodie of the National Heart Institute, National Institutes of Health, Bethesda, Maryland. The discourses are not only on absorption through various barriers—alimentary, blood-brain, and placental but also on a wider field, including experimental techniques, physiological and physicochemical factors related to drug absorption, their distribution and their ultimate fate in the body.

The factors of absorption and distribution of drugs are governed by physicochemical and pharmacological principles, true appreciation of which, are of significant importance both for the manufacturer and the clinician. This is perhaps the first attempt of its kind to collect together the available information on this very important subject through a conference of workers reputed for their basic research on medical and para-medical principles and through the co-operation of academic medicine and the pharmaceutical industry. In these days of tremendous development of new and highly potent drugs and remedies during the last two decades, it is now of paramount importance to know about their localisation and transport in the system. With the help of this knowledge it is now possible to overcome the undesirable systemic effects of a drug to varying degrees, by combining its active moiety with a suitable transport carrier, especially in cases of such drugs which are known to have a definite beneficial effect in diseased cells but which show high systemic activity, related to absorption, distribution or fate in the body.

This volume contains a wealth of information directly from the experts on the different aspects of the problem. This undoubtedly makes the work more interesting and valuable not only to pharmacologists but also to clinicians and administrators who control the administration of drugs to human subjects. This volume fills a big gap in our present knowledge about the metabolism of drugs, the available information having been presented briefly and precisely. There is an abstract with each paper, which will surely be found useful both for academic interest and reference.

A notable feature of this book is that about half of the contributions are from the pharmaceutical industries, persons who are the pioneers in the synthesis and introduction of newer products and hence, responsible for their primary screening and understanding of the actions of a new drug. It is to be admitted that the whole future of drug research depends on the degree of active co-operation and close scientific collaboration between industrial and academic research, between experimental, clinical and chemical pharmacologists and physicians, particularly related to paramedical disciplines. This type of symposium and publication is only the beginning of such an admission, and is therefore timely and welcome.

M. L. Chatterjee

OBITUARIES

Dr. Mannu Lal Sharma

Dr. Mannu Lal Sharma was born in 1877 in a respectable Brahmin family of Meerut District in U.P. He qualified as Hospital Assistant in 1903 from the Agra Medical School and was appointed a Sub-Assistant Surgeon under the U.P. Government. He did not take up private practice after his retirement in 1933 but spent his time in the service of educational institutions. He was associated with the management of a number of schools and colleges of Meerut. He took keen interest in the activity of A.I.M.L.A. and was Treasurer of its U.P. State Branch for over two decades. In May, 1964, he had a stroke resulting in hemiplegia of the left side of the body and died on January 20, 1965. He leaves behind a daughter and a large number of friends to mourn his loss.

Dr. Sudhir Kumar Ganguli

Death occurred at Hojai in the district of Nowgong, Assam, on 1-5-65 of Dr. Sudhir Kumar Ganguli, a senior medical practitioner and a social worker. He was 58.

Born in a respected family in Jessore in 1911, Dr. Ganguli came to Assam in 1934 and worked in several tea gardens till 1942. He finally settled down at Hojai in 1942.

An active member of the Hojai Branch of the I.M.A., Dr. Ganguli earned popularity among all sections of the people.

He leaves behind his wife, five sons and one daughter, and a host of friends and admirers to mourn his loss.

Dr. Radhakanta Goswami

Dr. Radhakanta Goswami was born on 22-9-1900 at Natore, District Rajsahi now in East Pakistan. After completing his early education in his home district, he joined the R. G. Kar Medical College (then Carmichael Medical College) and passed the Final M.B. Examination in 1932.

He joined the Hooghly District Board Dispensary at Kumrul in 1936 and served the local people for 11 years. Later he was transferred to Basudevpur District Board Dispensary where he worked till 1948. In 1949 he started independent practice at Tarakeswar and by dint of his amiable behaviour, sincerity of purpose and loving personality in a short time established a lucrative practice in Tarakeswar and the adjoining areas.

Dr. R. K. Goswami

In 1948 he started the branch of the Indian Medical Association at Tarakeswar and was elected Hony. Secretary of the branch. Due to his untiring efforts the branch grew from strength to strength and came to have 71 members on its roll. Dr. Goswami became the Vice-President of Bengal State Branch of the I.M.A. in 1964.

Dr. Goswami was a very reputed speaker and writer. He used to write poems and deal with various subjects of public interest in the periodicals and dailies.

He was connected with various educational institutions in Tarakeswar. In his death the profession, as well as the I.M.A., has lost a respected colleague and the public a beloved, benevolent and a popular doctor, who served them indefatigably all his life.

Dr. Goswami breathed his last on 4-8-65 under tragic circumstances on the streets of Calcutta. He passed away unknown, unidentified, untreated and away from near and dear ones.

He leaves behind his wife, two sons and four daughters and a host of friends and admirers to mourn his loss.

CORRIGENDUM

Vol. 45, No. 4, August 16, 1965 Issue

Page 207, Column 1, Line 5 from bottom :

In place of " . . . . . . serum calcium—19·8 mg. per cent" *please read* " . . . . . . serum calcium—10·8 mg. per cent".

SUPPLEMENT

Journal of the Indian Medical Association

Vol. 45, No. 7 CALCUTTA October 1, 1965

XLI ALL-INDIA MEDICAL CONFERENCE BARODA

I.M.A. General Secretary's Announcement Re: Railway Concession

Dr. Ved Prakash, Hony. General Secretary, I.M.A. in his Circular No. F.111/1/68/64-65 dated 25-8-65, addressed to the Hony. Secretaries of State/Territorial and Local Branches, members of the Working Committee and members of the Central Council of the I.M.A., states :

It is notified for general information that the Railway Board have agreed to grant the usual railway concession, i.e., single fare double journey for the forthcoming 41st Annual Conference of the Indian Medical Association to be held at Baroda from 28th to 30th December, 1965 on production of the requisite certificate from the Hony. General Secretary, I.M.A., New Delhi. The conditions of availing the concession are : (1) In the case of first class, the concessional return fare will be subject to a minimum of two single journey full first class fares for 400 kilometers; (ii) In the case of second and third class, the concession will be admissible for persons travelling beyond 400 kilometers from the place of the Conference without any minimum fare.

Since the certificate for railway concession has to be issued from the Headquarters Office, members desiring to avail of it should send the registration fee of Rs. 5/- by postal order (not by cheque or money order) to this office as early as possible when applying for the concession.

The following details must invariably accompany the request for the concession form : 1. Name in capital letters. 2. Address. 3. Name of the branch of the I.M.A. of which he/she is a member. 4. Number of postal order. 5. Name of Railway Station from which journey to and from Baroda is to be performed. 6. Fare of single journey to Baroda. [This is applicable to those members who are under the rules entitled to claim T. A from the I.M.A. (Headquarters)].

The concession is available for members of the Association only and not their families.

Members who are Government servants or employees of local bodies and statutory authorities and whose travelling expenses for journeys to and from the Conference are borne wholly or partly by their employers are not entitled to this concession.

I.M.A. COLLEGE OF GENERAL PRACTITIONERS

II Orientation Course in General Practice—1965

The Second Orientation Course in General Practice organised under the auspices of the I.M.A. College of General Practitioners will be held at the I.M.A. House, Indraprastha Marg, New Delhi, from Friday, October 15, to Sunday, October 17, 1965. Dr. Sushila Nayar, Union Health Minister, will inaugurate the Orientation Course on 15-10-65 at 9-10 A.M. at the I.M.A. House.

The State/Territorial Branches with membership below 1000 can depute 4 representatives and for every additional 1000 membership or part thereof 1 additional representative. Local branches are to forward the names of their representatives to their State/Territorial Branches for inclusion in the State Branch's representation. The representatives will be paid T.A. and D.A. as per rules framed for the participants in the Course. Besides the official representatives, other members of the I.M.A. can also attend the Course at their own expense.

The Inaugural Session of the Orientation Course will be held on 15-10-65 from 9 A.M. to 10-15 A.M. under the chairmanship of Dr. A. P. Mitra, President of the I.M.A. Dr. Sushila Nayar will speak on General Practice as an Essential Service. Dr. Ved Prakash, Hony. General Secretary, I.M.A. will propose the vote of thanks.

The detailed programme for the Course has been fixed as follows :

Friday, October 15, 1965

MORNING SESSION—10-30 A.M. TO 12 NOON

Chairman—Dr. C. L. Jhaveri, Sr. Vice-President, I.M.A.

Subjects—Patterns of Illness in General Practice. Some Common Problems in General Practice. Doctor-Patient Relationship.

Names of speakers to be announced later on.

AFTERNOON SESSION—2-30 P.M. TO 5-15 P.M.

Chairman—Dr. K. L. Wig, Director, All India Institute of Medical Sciences, New Delhi.

Subject—Training General Practitioners.

Subjects	Speakers
Pre-registration Training	Col. Amir Chand (Delhi)
In-practice Training	Dr. P. C. Dhanda (Delhi)

Subject—General Practitioners' Role in Teaching Programmes

Subjects—At Undergraduate Level. In Preceptorship Programme. In Hospitals. General Practice—Solo, Polyclinics, or Group Practices.

Names of speakers to be announced later on.

Saturday, October 16, 1965

MORNING SESSION—9 A.M. TO 10-30 A.M.

Chairman—Dr. K. N. Rao, Director General of Health Services, New Delhi.

Subject—Role of General Practitioner in the Field of Preventive Medicine.

Subjects—Immunological Problem in General Practice. Health Legislations in the Country and the General Practitioner. General Practitioner and Communicable Diseases.

Names of speakers to be announced later on.

MORNING SESSION (CONTD.)- 11-15 A.M. TO 12-15 P.M.

Subjects—Organising Diagnosis in General Practice. General Practitioner and New Drugs. Iatrogenic Diseases in General Practice.

Names of speakers to be announced later on.

AFTERNOON SESSION—2-30 P.M. TO 5-30 P.M.

Chairman—Dr. N. Banerjee (Calcutta)

Subject—General Practice and Consultant Practice.

Subjects—Field of General Practice. Field of Consultant Practice.

Names of speakers (one a general practitioner and the other a consultant) to be announced later on.

Subject—Orientation of General Practitioners in Psychiatric Problems in Practice.

Speaker—Dr. H. R. Ohri (Patiala).

Subjects—General Practice and Hospital Relations. General Practice—Value of Record Keeping for Research. General Practitioners' Role in the Care of the Aged and the Dying.

Names of speakers to be announced later on.

Sunday, October 17, 1965

MORNING SESSION—9 A.M. TO 11 A.M.

Chairman—Brig. Inder Singh, Medical Adviser, A.F.M.S., (New Delhi).

Subject—Emergencies and Their Management in General Practice.

Subject—Injuries, Burns and Accidents.

Speaker—Dr. J. L. Gupta (New Delhi).

Subjects—Coma. Colics and other Abdominal Emergencies. Hyperpyrexia. Anaphylaxis and Allergies.

Names of speakers to be announced later on.

MORNING SESSION (CONTD.)—11-45 A.M. TO 1-15 P.M.

Chairman—Prof. S. B. Roy, Professor of Cardiology, A.I. I.M.S., New Delhi.

Subjects—Dyspnoea and Respiratory Emergencies. Haematemesis and Haemoptysis. Pain in Chest.

Names of speakers to be announced later on.

AFTERNOON SESSION—2-30 P.M. TO 5 P.M.

Subject—Acute Dehydration.

Speakers—Dr. P. N. Taneja.

Subjects—Convulsions and Fits. Bleeding P. V. Eclampsia. E. N. T. Emergencies. Poisonings.

Names of speakers to be announced later on.

CONCLUDING SESSION—5-30 P.M. TO 5-50 P.M.

Chairman—Dr. A. P. Mittra, President, I.M.A.

Subject—I.M.A. College of General Practitioners and the Continuing Education of General Practitioners.

Speaker—Dr. P. C. Bhatla (Delhi).

XVIII GUJARAT STATE MEDICAL CONFERENCE : : ANAND : : 1965

The 18th Gujarat State Medical Conference was held at Anand in the Kaira District on May 1-2, 1965. The Conference was inaugurated by Sri Utsavbhai Parikh, Minister for Revenue and Agriculture, Gujarat State, and presided over by Dr. C. P. Munshi, President-elect of the I.M.A., Gujarat State Branch for the year 1965-66.

The Scientific Session organised on this occasion was inaugurated by Dr. C. S. Patel, President of the Medical Council of India.

Dr. R. R. Doshi and Dr. A. G. Patel were the Chairman and Organising Secretary respectively of the Reception Committee.

INAUGURAL SESSION

The inauguration of the Conference took place on 1-5-65 in the presence of a distinguished gathering of medical men and delegates coming from all over the State. According a hearty welcome to the guests and the delegates Dr. R. R. Doshi referred to the pride of place occupied by the city of Anand in the history of the national independence movement for once being the field of activities of Sardar Vallabhai Patel, the great patriot and valiant leader of the nation who was born at the village Karamsad only 6 miles away from this city. He then acquainted the gathering with some of the problems as well as the possibilities of the district. He spoke of the commendable progress made by the district in the sphere of education and cooperative dairy development. Of the two leading maladies—ankylostomiasis and tuberculosis—affecting the people here, the first had been brought under some control, he said, by the steps taken by the State Health Department. Curative and preventive measures for fighting tuberculosis had also been taken up by both the Government and voluntary organisations including the I.M.A., he said, and mentioned in this connection the important part the Mission Hospitals were playing in rendering medical relief to the people. What the district badly needed, he said, was a good civil hospital with different wings including one for coping with the medical problems in the industries. Dr. Doshi also stressed the need for setting up a medical college in the district for which he hoped help and assistance would be forthcoming from all quarters.

Sri Utasavbhai Parik then rose to inaugurate the Conference. Briefly referring to the measures the State Government were contemplating for improvement of medical care and expansion of medical education in the State he appealed to the delegates to extend their cooperation in implementing these schemes.

Following the formal inauguration of the Conference Dr. N. S. Shah, the outgoing President of the State Branch, installed Dr. C. P. Munshi in the presidential chair. Dr. Munshi then delivered his Presidential Address in course of which he dwelt on some of the vital issues confronting the medical profession in the State.

SCIENTIFIC SESSION

The Scientific Session was inaugurated on 1-5-65 and continued on the following day. Inaugurating the session Dr. C. S. Patel expressed his pleasure at being able to participate in the Conference and remarked in a reminiscent mood, "Looking around I see a number of very familiar faces, several of whom have been my colleagues in the profession and who have risen in the various fields that they have chosen". "Gujarat", he said, "has always been known as a progressive State. I am sure that the State Government appreciates the necessity of progress in medical education and medical relief". Reminding his audience that the Medical Council of India was making continuous efforts to increase the number of medical colleges and the number of students admitted to them without impairing the standard of medical education, Dr. Patel said that he was anxious to see that the name of our country was held on the top in the field of medical education and that our qualifications were given tht utmost respect and regard all over the world. Both for the purpose of attaining sufficient proficiency in medicine by assimilation of the newer knowledge and skill, and for finding effective means of cure and control of the diseases prevailing in our country, the sipirit of adventure involved in research was indispensable, he said. Stressing that this spirit of research should be inculcated in our students as early as possible, he said, "I feel that this can best be done by introducing our medical students to research even at the undergraduate stages and make them undertake studies on simple problems and prepare reports". He disclosed that in the revised undergraduate curriculum the Medical Council was laying stress on this aspect and also on

SRI UTSAVBHAI PARIKH, MINISTER FOR REVENUE AND AGRICULTURE, GUJARAT, INAUGURATING THE CONFERENCE

L—R : Dr. A. G. Patel, Organising Secretary; Dr. P. R. Trivedi, Hony. Secretary, State Branch; Dr. C. P. Munshi, President, State Branch (1965-66); Shri Parikh; Dr. N. S. Shah, President, State Branch (1964-65); Dr. C. S. Patel, President, Medical Council of India; Dr. R. R. Doshi, Chairman, Reception Committee; Dr. M. O. Vyas, Chairman, Scientific Committee

the aspect of integrated teaching whereby students could see for themselves .diseases in its various manifestations right from the beginning of their entrance into a medical college and study and associate for themselves the problems of social and environmental factors in diseases.

Srtessing the importance of research to progress in medical education and the need for providing adequate funds for the same Dr. Patel said, "Every teacher in the medical college should participate in research. I am even of the opinion that unless teachers produce some good research work they should cease to be teachers and assessment of the work done by them should be made every five years and they should be allowed to continue only if their work has been satisfactory". Referring to the hesitation on the part of young graduates to take up postgraduate training in basic sciences, which was one of the causes of shortage in the number of qualified teachers for the medical colleges, he said, "The reasons are quite obvious and it is for the Governments to remedy them". He admitted, however, that even with the opening of more postgraduate institutes the problem of shortage of trained teachers could not be easily solved because of the large requirement of specialists and the meagre training facilities available. Speaking of the reluctance of young medical men to go and serve the people in rural areas he said, "Having been trained to work with a number of facilities like help from the laboratory and the x-ray departments, they feel rather diffident without them. The question of accommodation and minimum comforts for doctors in these areas have to be solved. Additional remuneration or incentives should be given to help in getting more doctors to work in these areas". Dr. Patel expressed the view that service in such areas should be limited for a period of 2 to 3 years and every medical officer in service should be compelled to put in this service and no excuse or influence of any kind should be brought to bear to see that such postings are avoided by a few. Concluding Dr. Patel commended the arrangement of refresher courses by the I.M.A. to help doctors in brushing up their knowledge and to learn new trends in medicine. He, however, suggested that the refresher courses should not last for more than a week at a time and the main attempt should be to help practitioners with such knowledge as may be useful in their day to day work both in the field of diagnosis and treatment and also in the prevention of diseases.

PRESIDENTIAL ADDRESS

Dr. C. P. Munshi began his address with an appraisal of the achievements of Anand, the venue of the Conference, in the field of rural education embodied in its big rural university and in the field of cooperative endeavour exemplified in the Amul Dairy Ltd. In course of his address he said :

In the field of medicine, Anand has not lagged behind. My mind goes back to year 1949 and before, when a foreign missionary, Dr. Cook, made it a medical centre of renown. Many patients were attracted from all over Gujarat for his advice. He used to take part in conferences and contribute to the academic side of the medical profession. After his retirement the medical profession in Anand suffered an eclipse. It was difficult to fill the vacuum created by his exit. Slowly this gap was filled and there was a resurgence of medical profession. Holding of this Conference is a testimony to its revival. I can look back with pride for this state of affairs, that my own students have contributed in no small measure.

I have been a teacher for many years, and it is only too natural that medical education claims a priority in my discussions.

MEDICAL EDUCATION :

At present, the State of Gujarat has five medical colleges ; the latest one is at Surat. The total number of students admitted to these colleges in 1963-64 was 635. It is planned to admit 70 more in 1965 and bring the total to 705. Only fifteen years ago, there were two colleges and admissions were around 150. The increase is stupendous. It is natural that in this mass production to achieve the ratio of doctor to people 1 : 5500, the quality is the casualty. The aim of medical education is not only to produce doctors for medical relief but also to produce medical experts, teachers, administrators and researchers. It is for this that quality is a must. These four are the pillar of medical education. Medical science is advancing at a fantastic rate. The old conceptions are tumbling down, yielding place to new. It is difficult for a good student to keep pace with newer advances. This race is like Lewis's circus movement. In a case of mitral stenosis, he has not only to diagnose stenosis, but whether it is critical, or operable or there is a restenosis. In olden days diagnosis of mitral stenosis was the end in all. The same is the story with pharmacology. The other day I had a talk with a Professor of Pharmacology. He said that now we have not only a pharmacology for the pathological organs but a cellular pharmacology and the latest one, a molecular pharmacology.

In the present days, a physician or a surgeon is no less a victim to this advancement. He has not only to become a surgeon or a physician, he has to be a cardiologist, or a urogenital surgeon. I am reminded of a story where specialisation has travelled to the other extreme. An electro-cardiologist was given an E.C.G. to read. He read only P waves in that and sent it back with the remarks that for the reading of Q R S—complex it should be referred to its own expert. This is how medicine is moving, but in these countries the wind is sweeping back and the latest speciality is a general practice.

We are also affected by these changes ; setting up of cardiothoracic, neurological units and psychiatrical clinics and wards are the steps in this direction.

To achieve this end, we need to reorientate our medical education. Many efforts are being made in this direction. The period of medical education is increased, the post examination training is given, integrated teaching is introduced between clinical and preclinical subjects, preventive medicine is stressed especially to help our own problems. The examination system is altered and gradually a credit system is introduced to assess the students. All these new methods are aimed at improvement in education to meet the newer demands.

THE TYPE OF TEACHER :

The other change which is contemplated is that of the type of the teacher. The honorary system which is part-time is being replaced by full time teachers. It is presumed that the honorary system has outlived its utility and is a spent force. It should be discarded as it cannot meet the challenge of the present day teaching and research. I beg to differ here. I am privileged to belong to the honorary system. The honorary system has pioneered the medical education in this part of the country. Some, even with enormous medical practice outside the hospital, have voluntarily spared time for teaching at the college regularly. Even in the field of research, their contribution is no mean. It has won them national and international awards. Their names are too well-known to be mentioned. With increase in the demand for intensive teaching, the honorary system has adjusted itself to the newer condition and spared more time for teaching. In my institution, where W. H. O. project is working, the three honorary units are running specialised units in the afternoon, like gastro-enterology, cardiology and neurology. The teaching of postgraduates is done in extra-time, asking nothing more in return except goodwill. They take part in various newer teaching sessions like, symposia, panel discussions and lectures series. If properly handled, the honorary system can rise to greater heights and would yield excellent dividends.

For the full-time teachers the emoluments being meagre, compared to the type of work expected from them, the right type of persons are not attracted and if at all they join, they leave the place for better prospects elsewhere. Thus the frequent change of personnel does not fulfil the purpose for which this system is created. The pay scales should be as recommended by the I.M.A. Only a well satisfied teacher can fulfil all the obligations that devolve on him. In these days when the cost of living is rocketing, financial aspect cannot be a secondary consideration.

MEDICAL RESEARCH AND DRUGS TRIAL :

A problem closely allied with the medical education is medical research. Medical research does not mean only finding out fundamentally new. It is one aspect of the problem. It has many facets. One important aspect is working out the incidence of various diseases at various ages and sex-wise. This helps the medical practitioner in general for his clinical practice. Some years back it was thought that rheumatic heart disease is rare in India, but now we know it is a major cardiovascular problem in our country. In our cardiac department, it forms about ⅓ of cardiovascular problem. At present the major part of cardiac surgery is correction of mitral stenosis.

The other aspect is trial of drugs in our patients. Trial and the results in other country cannot fit into our patients. The drug has to be evaluated in our patients and in our environments. I remember, some years back when chloramphenicol came in the market, the dose was massive. Such a Himalayan dose very often produced vasomotor collapse, though the temperature came down in a few hours. One of my senior colleagues used smaller dose, it was cutting the coat according to the cloth, as supply was short. We noticed that fever came down gradually, and collapse was averted. From then on we have been using a smaller dose. The same is the condition for using hypotensive drugs. Our hypertensives respond to ridiculously low dose. All these pinpoint to the fact of forming our own norms for diseases and drugs.

Recently when we were working on the mortality statistics, it was revealing that tetanus headed the list of killers, and majority of victims were from villages. Here is a disease which is preventible by simple immunisation and education about the disease. The cost of treatment even for a single case of Tetanus is very high to the patient or to the State exchequer. A simple vaccination can save lives and a lot of State money. This type of statistical research and drug trial research does not need costly instrumentation or equipment and can be easily carried out.

MEDICAL CAMPS :

The medical camps have become a normal part of medical relief. It stands to reason that poorer section of the village population or the underdeveloped areas in the State which are inhabited by tribal people, where modern medicine has not penetrated, should be provided with medical relief camps. The camps not only afford medical relief but impart medical education. The tribal people are thus attracted to the medical centres near by. It was suggested by one of the past Presidents that a body be set up to organise and conduct such camps so that these could be conducted more efficiently and economically. Even the staff conducting such camps should be recruited separately for such work instead of drawing them from the neighbouring hospitals and disrupting the routine work. At present the yardstick of success seems to be the amount of work done. Later on the unrelieved patients trickle to the hospitals. I would suggest a proper follow-up of these patients regarding their relief and complications and mortality, early or delayed. The controlling body should also cater for this aspect which is a real basis of success. This will give a true perspective of the medical relief camps and their actual utility.

E.S.I. SCHEME :

It is gratifying that the Employee's State Insurance Scheme is introduced. Nobody will challenge the usefulness of this system. E.S.I. Act of 1948 forms the basis for implementation. It was first introduced in Kanpur. Gujarat is the last State to introduce this scheme.

I.M.A. has always favoured the panel system to the service system. Elsewhere and abroad the panel system is most favoured and it runs successfully looking after the interest of the patients and doctors alike.

The panel is like an institution of family physicians, and as such, rises above the rules of the scheme and gives its best. The doctor-patient relationship is maintained, and apart from treatment other advice, namely preventive, social, and occupational, is always forthcoming unsought for. This aspect of the scheme, which is its soul, can only be catered to by the panel system. This system is a financial gain to the State. A State which is a deficit one cannot lose sight of this aspect lightly. A State which has big health problems to tackle, like drinking water, disposal of sewage and stinking factory

Dr. C. P. Munshi

President, XVIII Gujarat State Medical Conference

effluents, health education and school health service, can ill afford to dissipate its resources if other alternatives are available. It is too early to comment on the working of the scheme, as it is in its infancy. Teething problems are always there, and they can be overcome by goodwill on all sides. Best advertisement of panel system is the doctor himself and his work. No good work can go unrecognised, it is bound to proliferate. I appeal to the medical men who are manning this system to make it a grand success, so that their work would serve as a self-advertisement.

Recently when I was travelling from Poona to Bombay I met a doctor in the train who was a doctor in E.S.I. panel scheme. He told me that in urgent cases they never look to any aspect except the well-being of the patient which was their sole concern and many a time they were out of pocket, helping the patient. This is the real spirit of the panel doctors.

A PROUD PRIVILEGE :

In the end, I am sure I voice the sentiments of all the medical men, when I quote the words of Professor Gerhard Domagk, "The Life which I have been privileged to lead as a doctor has been a very wonderful and a very beautiful experience. I have had the constant support of colleagues whose enthusiasm equalled my own and whose one guiding principle both in their medical work and in their own lives, was service to others. This is a blessing for which I never cease to feel gratitude, and, were my life to be lived again, I would again become a doctor."

We are menaced on our frontier since the last few days. The Kutch border has become live. Our brave Jawans are laying down their lives to protect our motherland. In this hour of travail, I assure the Government and our Jawans, on behalf of the medical men of Gujarat, that we shall always lend our fullest support in helping them with our skill and resources.

BRANCH NOTES

BANGALORE BRANCH—A scientific meeting was arranged on 20-1-65. Dr. V. G. Sidenur, a member of the branch spoke on Fundamentals of Modern Genetics. Dr. M. Basavaraju, Professor of Physiology, Bangalore Medical College, presided over the meeting.

On 26-2-65 another scientific meeting was arranged in the M.M.A. Hall with Dr. Mrs. Ranee Christopher in the chair. Dr. H. R. Basavaraj, Health Officer, Health Training Centre and Government of India Family Planning Training Demonstration and Experimental Centre, Ramanagaram, spoke on Facts on Intrautrine Plastic Devices.

A special meeting was held on 19-3-65. Dr. B. N. Lingaraju, Dean, Bangalore Medical College, presided. Prof. B. V. Raman, Editor, Astrological Magazine, Bangalore, spoke on Astrology as an Aid to Medical Science.

BETTIAH BRANCH—The Bihar Health Week was successfully observed by the branch on 7-3-65. The programme was inaugurated by Shree K. N. Sahay, S.D.O. (Civil), Bettiah. Popular lectures were given by Dr. G. Singh, Dr. K. K. Gupta, and Principal B. N. Jha of the M. J. K. College. This was followed by the inauguration of the Health Exhibition.

On 9-3-65 there was a day-long programme at Chanpatia Block where besides holding of a baby show, school health examination and popular lectures, a number of vasectomies was done.

On 11-3-65 the baby show held at Bettiah drew a large crowd.

On 13-3-65 the community health programme received high appreciation from the public. A batch of twelve male doctors and three lady doctors conducted the clinic for the males and the females respectively. About two hundred persons were examined systemwise by different doctors. The check-up included eye and urine examinations. Recorded findings with complete advice were handed over to each person to his or her great satisfaction.

On different days members of the branch addressed the students of the local educational institutions on popular health subjects.

BHABUA BRANCH — The branch celebrated the Health Week on March 7-13, 1965. The opening ceremony was performed on 7-3-65 in the Child Welfare Maternity Centre, Bhabua, by Dr. Dukhan Ram, Ex-Principal of the Patna Medical College and Hospital. Sri M. Abdullah, S. D. O. (Civil), Bhabua, presided over the function.

Dr. A. S. Prasad, Hony. Secretary of the branch, spoke briefly on the health problems of the locality and the programme chalked out for the Health Week. Following him, the S.D.O., Dr. D. Ram and Dr. B. N. Prasad, Deputy Superintendent of the Subdivisional Hospital, spoke on the significance of the Health Week The function closed with a vote of thanks by Dr. B. N. Prasad.

A baby show was organised at the Bhabua Child Welfare and Maternity Centre on 9-3-65 in which 107 children participated. Prizes were distributed to ten healthy children by Mrs. M. Abdullah.

119 School children were also examined during the Week by Dr. B. N. Prasad and Dr. Mrs. Manorama Prasad of the Sub-Divisional Hospital, Bhabua.

The vaccination drive, the family planning campaign, and the community health drive covering 47 houses were undertaken in three villages under the Bhabua Block. Dr. A. S. Prasad, Hony. Secretary, and the Medical Officer for the Bhabua Block, along with members of the health staff conducted the above programme.

Films on health were also shown in the premises of the Bhabua Block to a large number of people.

CANNANORE BRANCH—A clinical meeting was held in the district hospital, Cannanore, on 21-3-65 with

Dr. P. I. Jacob, President of the branch in the chair. 28 members attended.

After the President's introductory remarks the Hony. Secretary read out the minutes of the previous meeting, which were confirmed.

Dr. C. E. Ooman, eye-specialist, District Hospital, Cannanore, demonstrated several cases of acute conjunctivities, iritis, glaucoma, keratomalacia, trachoma, macular choroiditis, optic neuritis, and cases with muscular imbalance and errors of refraction. He dealt with important points which were useful to the general practitioners. His demonstrations were followed by lively discussions in which a number of members took part.

The Hony. Secretary next read out the resolutions passed in the 8th Annual Conference of the Kerala State Branch at Trivandrum and the replies received thereto from the Kerala Government. It was decided that the branch should offer its comments on the above after holding a meeting of the general body next month, since sufficient notice could not be given to the members for considering different aspects of the proposals.

A resolution from the Alleppey branch of the I.M.A. was then placed in the meeting.

It was decided to appoint a sub-committee consisting of Drs. P. I. Jacaob, P. Rohini and K. P. Deveky to answer the questionnaire received from the I.M.A. Headquarters, Delhi, on Legalisation of Abortion.

Dr. P. Madhavan was the host for the day. Following the vote of thanks by the Hony. Secretary, the meeting came to a close.

CHAPRA BRANCH - A meeting was held on 20-3-65. The letter dated 5-3-65 from the Hony. Secretary, Bihar State Branch, was considered and a resolution was passed endorsing the steps proposed by the State Working Committee to demonstrate its support and sympathy for the members of the Medical and Health Services Association, if the latter were compelled to tender resignation due to non-implementation by the Government of the recommendations of the I.M.A. and the Health Services.

The meeting passed another resolution expressing its grave concern and resentment at the recent happenings at Dhanbad which caused much sufferings to some members of the medical profession and condemning the failure of the authorities to protect their person, property and prestige. The resolution stated that what had happened at Dhanbad had been narrowly averted in the Sadar Hospital at Chapra in 1962 and the same thing was occurring in many other places, where students were instigated by interested persons and parties by misrepresentation of facts, as was the case in Dhanbad. To root out this disease, the resolution affirmed, the Government should take stringent measures not only against the indisciplined students but also against the parties and persons responsible for creating such troubles.

DUMKA BRANCH —A general body meeting was held on 20-12-64 in connection with the observance of Bihar Health Week from 7-3-65 to 14-3-65. A proposal was passed suggesting the formation of the local Health Week Committee with the Deputy Commissioner, Santhal Parganas as the President, the Civil Surgeon, Santhal Parganas as the Vice President, Dr. C. P. Sinha, Hony Secretary of the Dumka branch as the Secretary and Treasurer. The names of the District Medical Officer of Health, Dumka, the Assistant Medical Officer of Health, Dumka Municipality and Dr. V. Thakur, Joint Secretary, I.M.A. Dumka branch, were proposed as Joint Secretaries. The names of 14 other persons who were drawn from all walks of life in Dumka were proposed as members. It was decided that in case of any member declining to accept office due to unavoidable difficulties, the Hony. Secretary of the branch might make necessary alterations. The active cooperation of all members was sought in making the programmes successful.

At a meeting of the Health Week Committee held on 27-2-65 under the chairmanship of the Deputy Commissioner, Santhal Parganas, a programme was chalked out in detail. The programme included sample survey of school boys and demonstration of family planning measures in Jama Block, inoculation and sanitation drive in the Municipal areas, school health examination at Guhiajori Mission, exhibition of health films, refresher course lectures and baby show.

It was decided to approach the Bihar State Health Week Committee for supply of milk powder and multivitamin tablets for distribution among the needy people, particularly, among the poor Adibasis. The Health Week was inaugurated at Jama on 7-3-65 by the Deputy Commissioner, Santhal Parganas, before a gathering of about 10,000 people. The speakers, who addressed the gathering, mainly dwelt on the state of health and the deficiencies observed in the school students under the Jama Block. The meeting closed with Santhali dance presented by the local team which took part in the Delhi Republic Day functions this year. In the evening films on health were shown.

From 8-3-65 to 14-3-65 inoculation against cholera and vaccination against smallpox were undertaken on a large scale by the municipal health staff, the district board health staff, and members of the I.M.A. During the sanitation drive launched in the municipal areas of Dumka, when doctors themselves started cleaning the slums and the drains, great enthusiasm was marked among the spectators. The Health Week ended with a baby show on 14-3-65 when about 500 babies were examined and prizes were distributed to the first three healthy babies in each group.

Refresher course lectures were given each evening by the members of the branch. A symposium on the local health problems was also held.

GHATKOPAR BRANCH —The annual meeting was held on 5-12-64 under the chairmanship of Dr. P. D. Daftary. At the outset Dr. M. A. Panwala, Hony. Secretary, placed the report for the year 1963-64.

The branch had completed seventeen years of its existence. In the beginning of the year under review the branch had 110 members on its roll. The number rose to 126 at the close of the year.

The activities of the branch were conducted by the following office-bearers: President—Dr. P. D. Daftary; Vice-Presidents—Dr. K. G. Phulwar and Dr. M. P. Trivedi; Hony. Secretary—Dr. M. A. Panwala; Hony. Joint Secretaries—Dr. K. R. Gandhi, Dr. G. M. Gandhi and Dr. P. B. Budwaik; Hony. Treasurer—Dr. K. H. Udani; Managing Committee Members—Dr. Miss Chandraben L. Shah, Drs. I. S. Pratap, M. T. Matkar and R. G. Chudgar.

The annual function was held on 23-2-64. Dr. V. S. Oak, President of the Bombay Territorial Branch, Dr. C. S. Thakar, a past President of the I.M.A., Dr. C. L. Jhaveri and Dr. Arvind Shah, among others, graced the occasion by their presence. The programme for the day included light games followed by a dinner, which was largely atended by members and their families, and exhibition of documentary films.

During the year the branch had organised, by the courtesy of the Rotary Culb of Bombay, an oral polio vaccine campaign. About one thousand children were given the vaccine in two successive doses, the first on 2-264 and the second on 15-3-64.

Camps for rendering medical relief to the people were also organised by the branch in cooperation with the Rotary Club of Chembur. Members of the branch also took part in the campaign for oral polio vaccine launched by the Lions Club of Ghatkopar.

The branch was represented in the All-India Medical Conference held at Madras in December, 1963, by Dr. P. D. Daftary, President of the branch and Dr. G. M. Gandhi, member of the Central Council, besides Dr. M. A. Panwala, who was also the Hony. Secretary of the Bombay Territorial Branch.

Thanks to the efforts of the Clinical Secretaries, the monthly clinical meetings were held regularly throughout the year. The meetings of the Managing Committee were held by turn in the residences of different members.

The branch played its due part in voicing the resentment among the doctors over the Government's attempt at imposing more restrictions on doctors and opening service dispensaries under the E.S.I. Scheme.

The branch also lent support to the Insurance Medical Practitioners when they were perturbed by the recognition of the factory utilisation services by the Government.

The above annual report was passed in the meeting, following which the election of office-bearers for 1964-65 took place. Managing Committee: President — Dr. M. A. Panwala; Past-President (*ex-officio*)—Dr. P. D. Daftary; Vice-Presidents Dr. K. G. Phulwar and Dr. M. P. Trivedi; Hony. Secretary—Dr. K. R. Gandhi; Hony. Joint Secretaries—Drs. R. G. Chudgar, G. M. Gandhi and P. B. Budwaik; Hony. Treasurer—Dr. K. H. Udani; Managing Committee Members—Drs. M. T. Matkar, I. S. Pratap, D. K. Tank and Dr. Miss. Chandraben Shah.

GUNTAKAL BRANCH—A meeting was held on 1-11-65 with Dr. K. Venkateswara Rao in the chair. Dr. H. M. Rao, D.M.O., Anantapur, delivered a lecture on Infection of Hand and its Management. Dr. Fiaz, a physician from Anantapur, spoke on Hypertension. With a vote of thanks by Dr. I. A. Ram Singh, Hony. Secretary, the meeting ended.

The general body meeting was held on 27-2-65. The following office-bearers were elected for the year 1964-65: President—Dr. K. Venkateswar Rao; Vice-President—Dr. K. V. Subba Rao; Hony. Secretary—Dr. I. A. Ram Singh; Hony. Joint Secretary and Treasurer—Dr. A. Seshagiri Rao; Representative to the State Council—Dr. P. Hemadri Rao; Representative to the Central Council—Dr. B. K. Nag.

INDORE BRANCH—A clinical meeting was held on 26-2-65. Dr. G. A. Kher, President of the branch, was in the chair. A case of atlantoaxial dislocation following trauma which needed operative interference because of recurrence was presented by Dr. R. K. Moorthy. The second case presented was one of multiple myeloma with paraplegia, which improved satisfactorily on endoxan therapy. Dr. B. K. Dhir presented a case of unilateral aphakia resulting from removal of iron particle F.B. in one eye with the help of a giant magnet. He discussed the suitability of contact lenses in such a case. A case of keratoplasty was also shown. Dr. M. S. Dwivedi presented a case of Ewing's sarcoma arising from a rib which gave rise to pleural effusion and was subsequently treated with endoxan with immediate good results. The other case was of urinary infection in a child associated with congenital anomaly of kidneys and ureters. Dr. K. L. Bandi showed a case of ureteric calculus and discussed the modern method of its removal. The meeting closed with tea arranged by Dr. R. D. Patwardhan.

KOZHIKODE BRANCH—The Working Committee of the branch met on 4-1-65 to consider its programme of activities for the next three months. The Hony. Secretary was authorised to take steps to arrange combined meetings with other branches. It was also decided to start a College of General Practitioners and to take active part in family planning activities when funds for the same would be available.

With Dr. C. K. Menon in the chair, a clinical symposium was held on 17-1-65 on Hypertension. Dr. T. D. G. Pillay acted as the moderator. Dr. V. Balakrishnan, discussed the aetiology and diagnosis. Dr. R. Govindan Nair discussed the drugs which are used in the treatment of hypertension. Dr. Unni stressed the problem of renal hypertension and mentioned the indications for surgery. Dr. Susan George spoke on the Clinical Management of Pregnancy Associated with Hypertension. Dr. T. D. G. Pillay summed up the discussions.

Earlier, Dr. P. B. Menon had demonstrated a typical case of Marfan's Syndrome with cardiac anomaly and subluxation of the lens. The meeting closed with a vote of thanks to the speakers and the chair.

A meeting was held jointly with the North Malabar Branch at Calicut. Dr. Capt. A. B. Das presided. Dr. T. K. Narayanan, President of the North Malabar branch, opened the meeting with a brief speech stressing the necessity for closer co-operation between the various branches of the Association. Following this, a number of interesting clinical cases were presented. Dr. R. Govindan Nair presented a case of pyrexia of unknown origin. Dr. C. B. C. Warrier showed x-ray plates of patients with various types of special compression, all demonstrated by myelograms. Dr. A. Thyagarajan presented a case of chronic ulceration of the ankle region in a patient with gigantism of the lower limb due to arteriovenous fistula. Dr. P. K. Abdul Gafoor demonstrated x-ray plates of a patient with spinal arachnoiditis. Dr. N. Mohandas presented a case of arthrodesis of the ankle for paralytic calcaneus deformity and a case of posterior spinal fusion for tuberculosis of the spine. Dr. N. S. Nair presented a case of typical Turner's syndrome demonstrating some of the well-recognised features. Dr. M. G. Sahadevan presented a case of tabes dorsalis.

A clinical lecture was held on 14-2-65 with Capt. A. B. Das in the chair.

It was decided that Dr. P. B. Menon's name should be proposed as a nominee of the branch to attend the September meeting of the British Medical Association.

Following this Dr. V. J. Nair gave a talk on Swellings of the Thyroid Gland. The talk was followed by a discussion in which many members took part.

A combined meeting was held on 28-2-65 at Malampuzha on the invitation of the Palghat Branch. The main feature of the meeting was a well-attended symposium on Jaundice. Speakers from Calicut, Palghat and Coimbatore took part in the symposium. The members present were entertained to a dinner at the end of the meeting.

A clinical meeting was held on 7-3-65. Dr. C. B. C. Warrier demonstrated a case of idiopathic cardiomyopathy occurring in the puerperium. He illustrated his subject with the help of x-ray plates and electrocardiographs. Dr. N. Rajan presented a case of Hashimoto's thyroiditis in which biopsy of the isthmus showed evidence of massive lymphocytic infiltration. Dr. R. Govindan Nair showed photographs of a patient with nephrotic syndrome treated with cortisone.

Dr N. Mohandas demonstrated an x-ray of an osteolytic lesion affecting the humerus which on histopathology showed appearances suggestive of epidermoid carcinoma. The primary could not be detected.

On 21-3-65 a clinical lecture was held with Capt. A. B. Das in the chair. At the outset Capt. Das introduced the guest speaker Dr. M. Srinivasan, Associate Professor of Surgery at the Kasturba Medical College, Mangalore.

Dr. Srinivasan gave an instructive talk on Surgical Emergencies in General Practice. He discussed the problems of diagnosis and management of emergencies in remote centres and illustrated his talk with slides.

The lecture was followed by a dinner at the Beach Hotel.

LUCKNOW BRANCH—The Third Refresher Course for General Practitioners was inaugurated on 13-3-65 by Dr. M. M. S. Siddhu, M.P., President, U.P. State Branch of the I.M.A., in the Pathology Auditorium of the K. G. Medical College, Lucknow.

Commending the idea of refresher course, Dr. Siddhu said that the general practitioner must be kept informed of the latest developments in medical science, otherwise the public would suffer. He suggested that the general practitioners should be attached to certain hospitals. He requested the doctors to attend seminars in cities where medical colleges were located.

Dr. Siddhu advised the medical graduates who had done the five year course not to be upset over the new arrangements of one year housemanship and to await the redress by the Government of their grievances.

Earlier Dr. N. N. Gupta, President, I.M.A., Lucknow Branch welcomed Dr. M. M. S. Siddhu and the participants.

Dr. R. V. Singh, Principal, K. G. Medical College, Lucknow, in his speech stressed the need of such courses which gave the opportunity of bringing medical practitioners in touch with the specialists of the medical colleges and thus helping them to increase their knowledge.

MARGHERITA BRANCH—A clinical meeting was held on 25-3-65 with Dr. B. K. Goswami, President of the branch in the chair.

The proceedings of the last meeting were read and confirmed.

Dr. S. N. Chatterjee, Medical Superintendent, A. R. & T. Co., Ltd., Margherita, demonstrated a case of intracapsular fracture of neck of the femur, which was successfully treated with three flanged Smith-Petersen nail under radiographic control. He then dealt with the different types of fracture of neck of femur and their treatment with a special description of the newest conception of the blood supply to the head and neck of the femur through branches of the medical circumflex femoral artery. Dr. M. C. Khaund demonstrated a case of postpartum acute dilatation of the stomach with retention of urine.

The meeting terminated with a vote of thanks proposed by Dr. B. B. Ghosh, the Hony. Secretary.

MORENA BRANCH—A meeting of the doctors of Morena (M. P.) was held on 5-2-65 in the Civil Hospital, Morena, to form a branch of the I.M.A. The following resolution was passed: Resolved that a branch of the Indian Medical Association be formed with immediate effect.

The following members were unanimously elected as the first office-bearers of the branch: President—Dr. P. N. Pathak, Civil Surgeon; Vice-President—Dr. Vijay Singh; Hony. Secretary—Dr. K. L. Rathi; Hony Joint Secretary—Dr. N. C. Bansal.

MOTIHARI BRANCH — An ordinary meeting was held on 28-3-65 at the residence of Dr. Hari Shankar Prasad. Dr. Prasad took the chair. 12 members were present.

The proceedings of the previous meeting were read and confirmed.

Dr. Kamta Prasad, Dr. M. Z. S. Quraishi, and Dr. G. K. Mishra were welcomed as new members.

The following resolution on the incidents at the Dhanbad Civil Hospital was passed unanimously:

The members of the Indian Medical Association, Motihari Branch, place on record with deep concern, the sad and unhappy incident of Dhanbad Civil Hospital in which a number of members of the medical staff and doctors were manhandled, their family members assaulted, and their properties damaged.

The members further resolve that a copy of this resolution be sent to the Hony. Secretary, Bihar State Branch of The Indian Medical Association, Patna, with a request to take up the matter with the State Government so that a judicial probe is instituted, especially, in respect of the failure on the part of the local administration to provide adequate protection to the hospital staff, the doctors and their family members, and the offenders are punished severely.

A symposium was held on the diagnosis and management of an unconscious patient. Dr. Manzoor Ahmad, Dr. M. Alam and Dr. Ram Sewak Singh were the main speakers. Other members also participated in the discussions.

An interesting case of rheumatic heart disease with mitral stenosis was demonstrated by Dr. Ram Sewak Singh. All the members examined the case and expressed their valuable opinion.

The members present were treated to tea by Dr. Hari Shankar Prasad.

The meeting dispersed with a vote of thanks to the host.

ORISSA STATE BRANCH—In the annual meeting of the Council of the State Branch held at Burla on 30-1-65 the following office-bearers were elected for the year 1964-65: President—Dr. R. N. Misra; Vice-President—Dr. S. Acharya; Hony. State Secretary—Dr. G. B. Mohanty; Hony. Joint Secretaries—Cuttack Zone: Dr. Mrs. N. Rath, Berhampur Zone: Dr. S. Bhimaraju, Burla Zone: Dr. B. K. Nanda, Rourkela Zone: Dr. S. Samantaray; Auditor—Dr. U. K. Nanda; Member of the Central Working Committee—Dr. R. N. Misra, Burla; Alternate member—Capt. K. J. Somayajulu, Jaypore.

RAMGARH BRANCH — The Bihar Health Week, 1965, was duly observed by the Ramgarh branch from 7-3-65 to 14-3-65.

During the week mass inoculation against T.A.B. and mass vaccination against smallpox were conducted throughout the Ramgarh Cantonment area jointly by the members of the branch and the local health authorities.

Examination of the health of students was undertaken on 11-3-65 and 12-3-65 in the schools. About 600 students were examined and reports on their health submitted to the headmasters for transmission to their respective guardians.

On 13-3-65 about 2500 students—boys and girls—of the different educational institutions of Ramgarh marched in procession along the main thoroughfares with posters and banners and raised slogans suggestive of the significance of the Health Week.

On 13-3-65 refresher course lectures for the members of the branch were delivered by Professor B. Prasad and Professor P. S. Jaiswal, both from the Ranchi Medical College, at the Regional Hospital, Naisarai.

On 14-3-65 a baby show was organised at the Ramgarh Cantonment Hospital. Out of the 75 babies of the town who participated, 9 babies were selected by the judges for award of prizes.

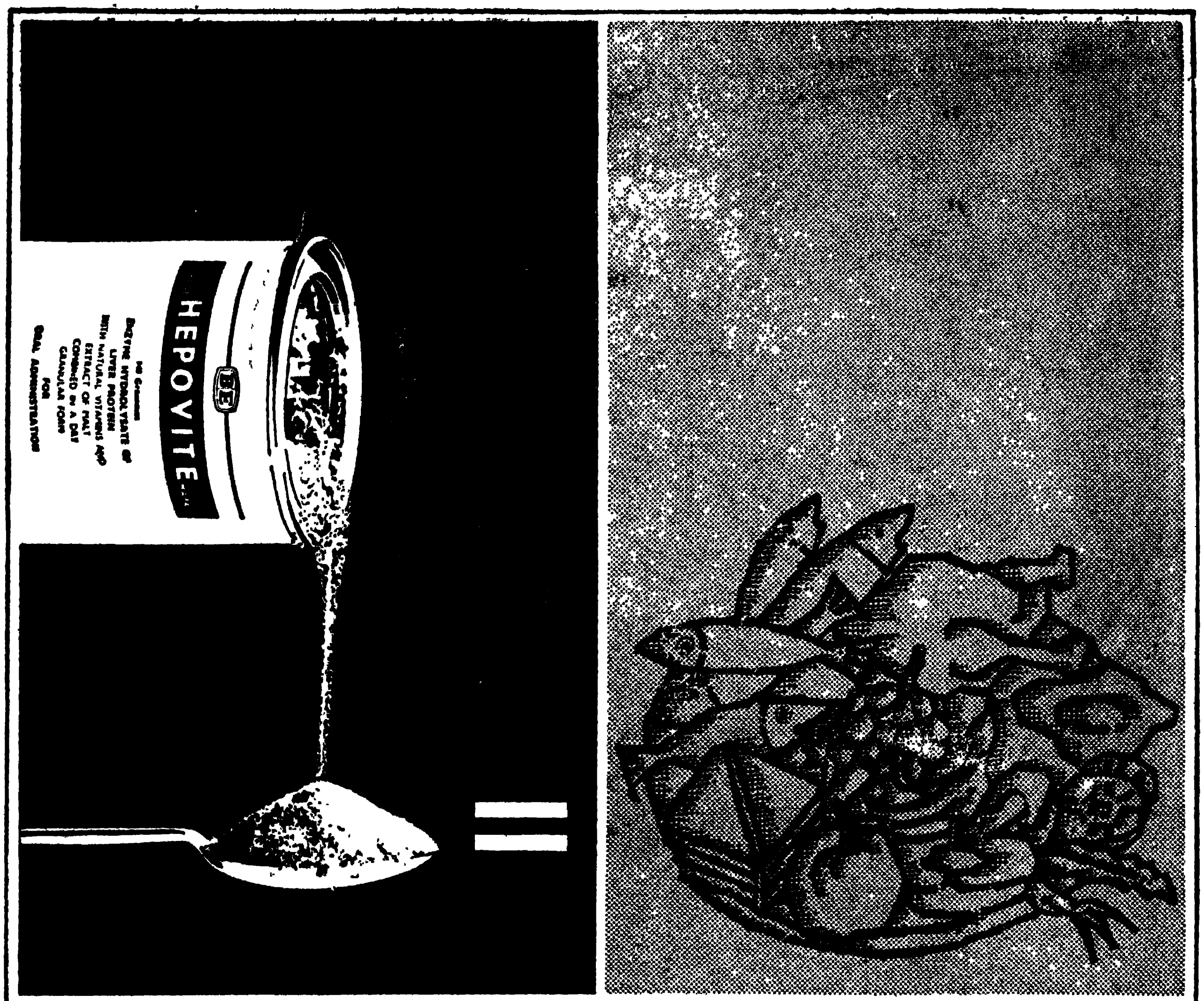
The closing function of the Health Week was held on 14-3-65 in the Gandhi Memorial School. Sri S. N. Panghia, B.D.O., Ramgarh, presided over the function, which was well attended. Popular lectures on public health were delivered by some teachers of the local schools. Dr. L. P. Chowdhuri, President of the branch, spoke on the utility of the Health Week. Dr. N. K. Shyam, Hony. Secretary, presented a report of the work done during the week. In his presidential address Dr. S. N. Panghia gave a brief account of the work done by the members of I.M.A. towards eradication and prevention of diseases like malaria, filaria, plague, smallpox, cholera, etc. The meeting ended with a vote of thanks by Dr. A. Raha, Joint Secretary, Health Week Committee.

TOLLYGUNGE BRANCH—Under the supervision of the branch a Child Health Exhibition was organised by the Ramkrishna Pallimangal Samiti in the premises of the Vivekananda Vidyapith, Jadavpur, Calcutta. The competition was held among children who were divided in three age-groups, namely, Group A for infants aged up to 1 year, Group B for children aged between 1 year and 3 years and Group C for those aged between 3 and 5 years. Medical examination of the competitors was done by the following members of the branch, besides Dr. B. C. Das, Hony. Secretary, who was the chief examiner: Drs. A. P. Das Gupta, D. P. Chakraborty, G. N. Biswas, N. K. Nath and C. R. Karmakar.

XVI M.P. STATE MEDICAL CONFERENCE : : UJJAIN : : 1965

Dr. A. C. Gaur, Organising Secretary, 16th M.P. State Medical Conference announces:

The 16th M.P. State Medical Conference will be held at Ujjain on October 15-17, 1965. The Governor of M.P. will inaugurate the Conference on 15-10-65. About 200 delegates from all over M.P. are expected to attend the Conference. Besides Scientific Sessions where about 25 papers will be presented for discussion, a Symposium will be held on Coronary Artery Disease on 16-10-65 under the chairmanship of Dr. V. V. Shah of Bombay. A Souvenir is also being published on the occasion.



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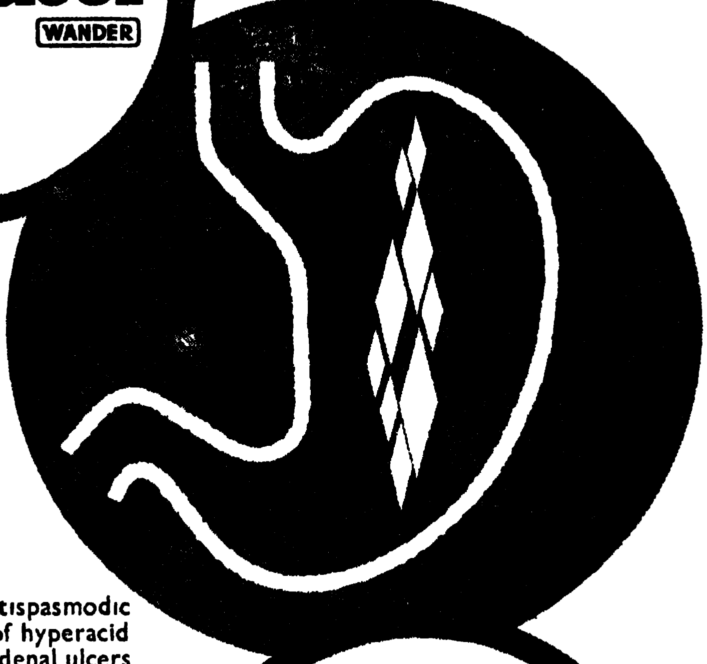

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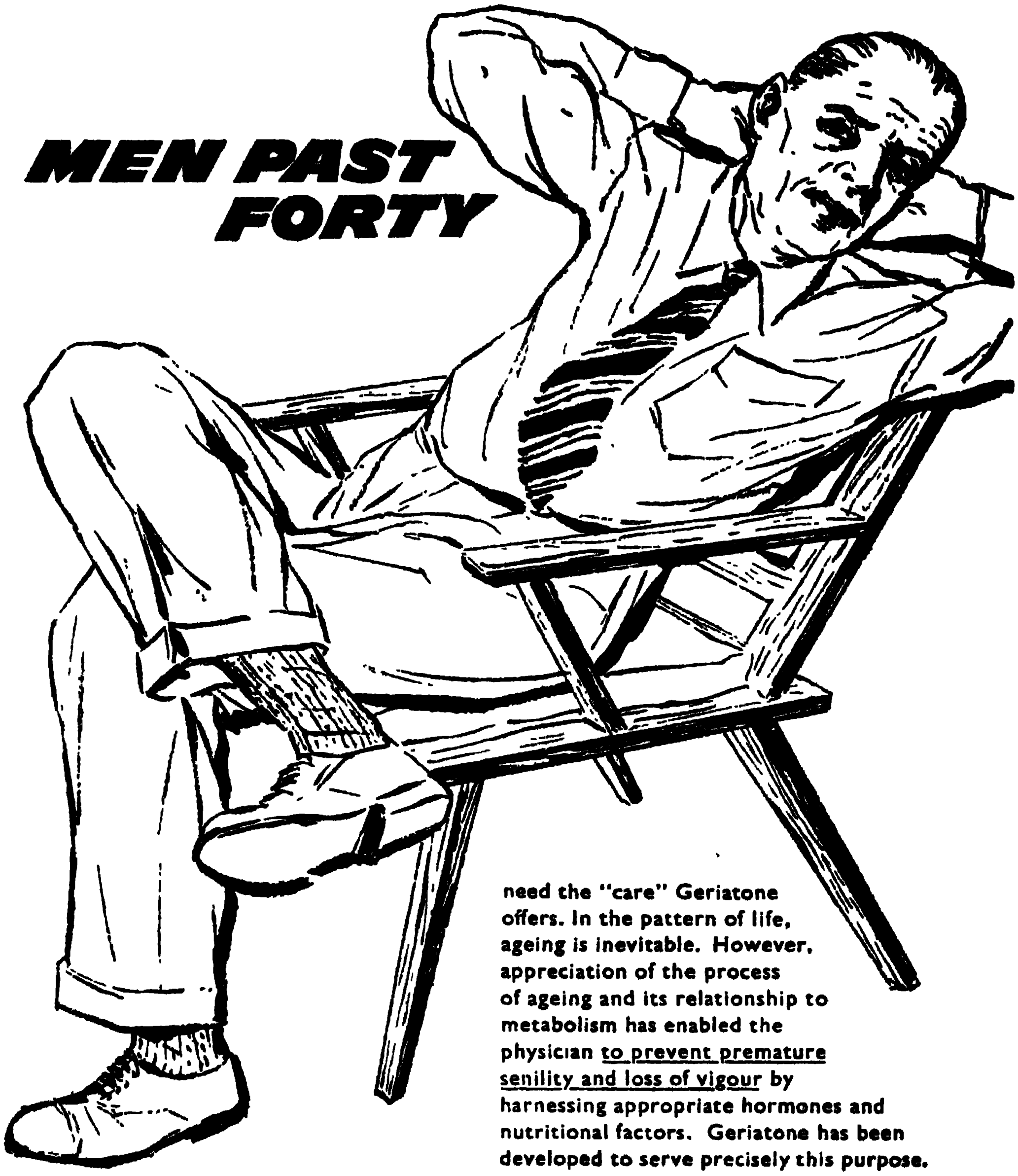

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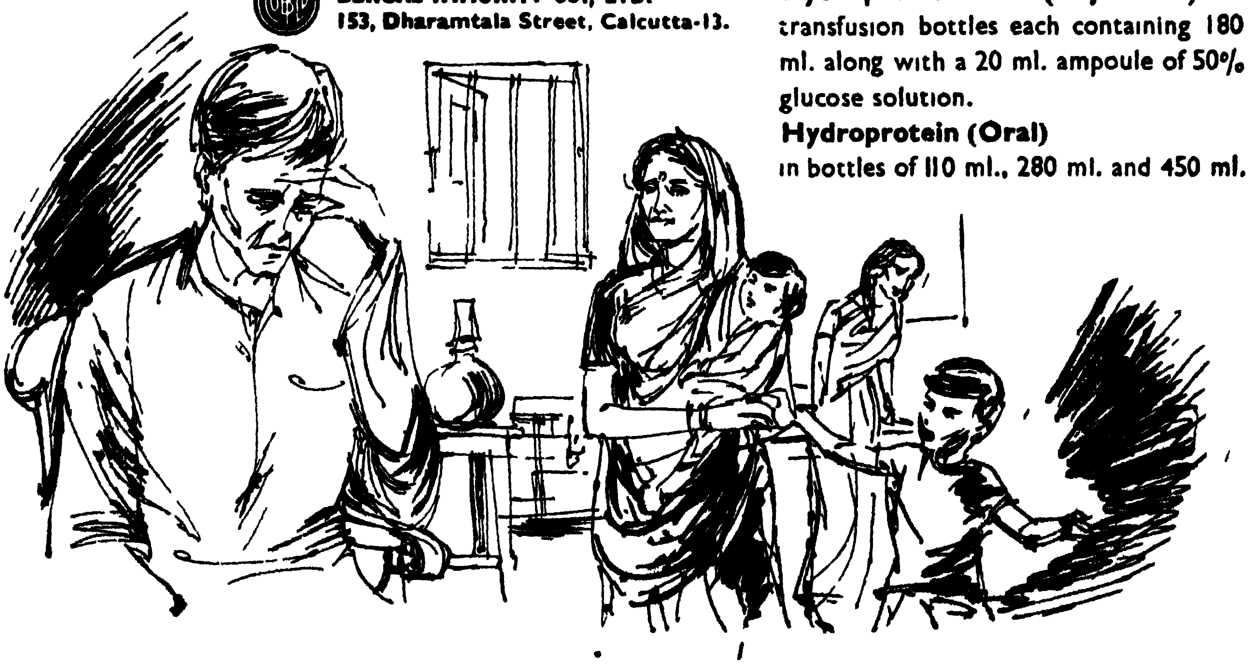

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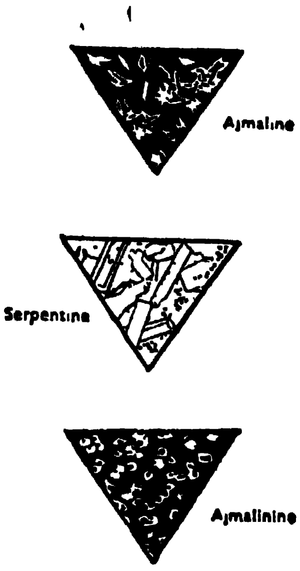

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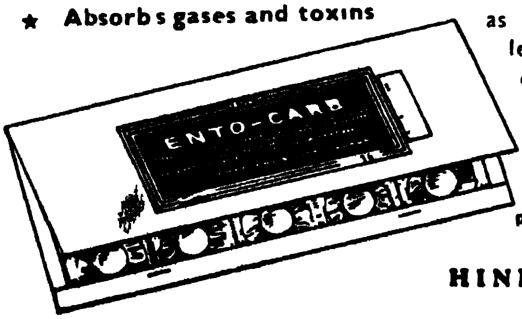

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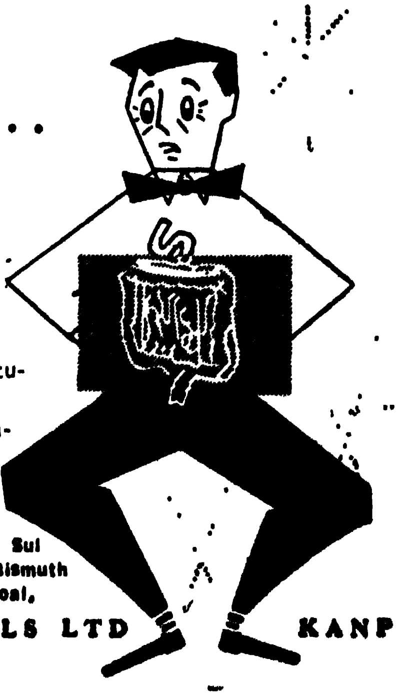

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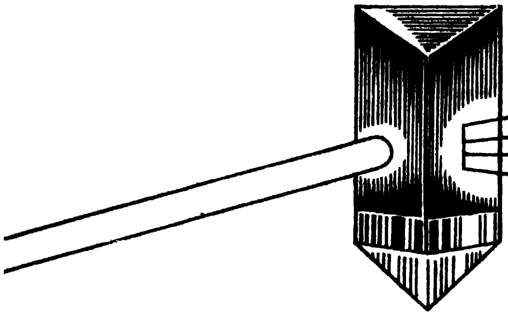

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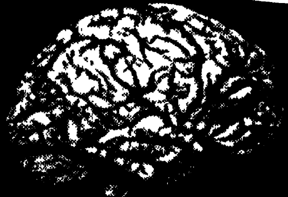

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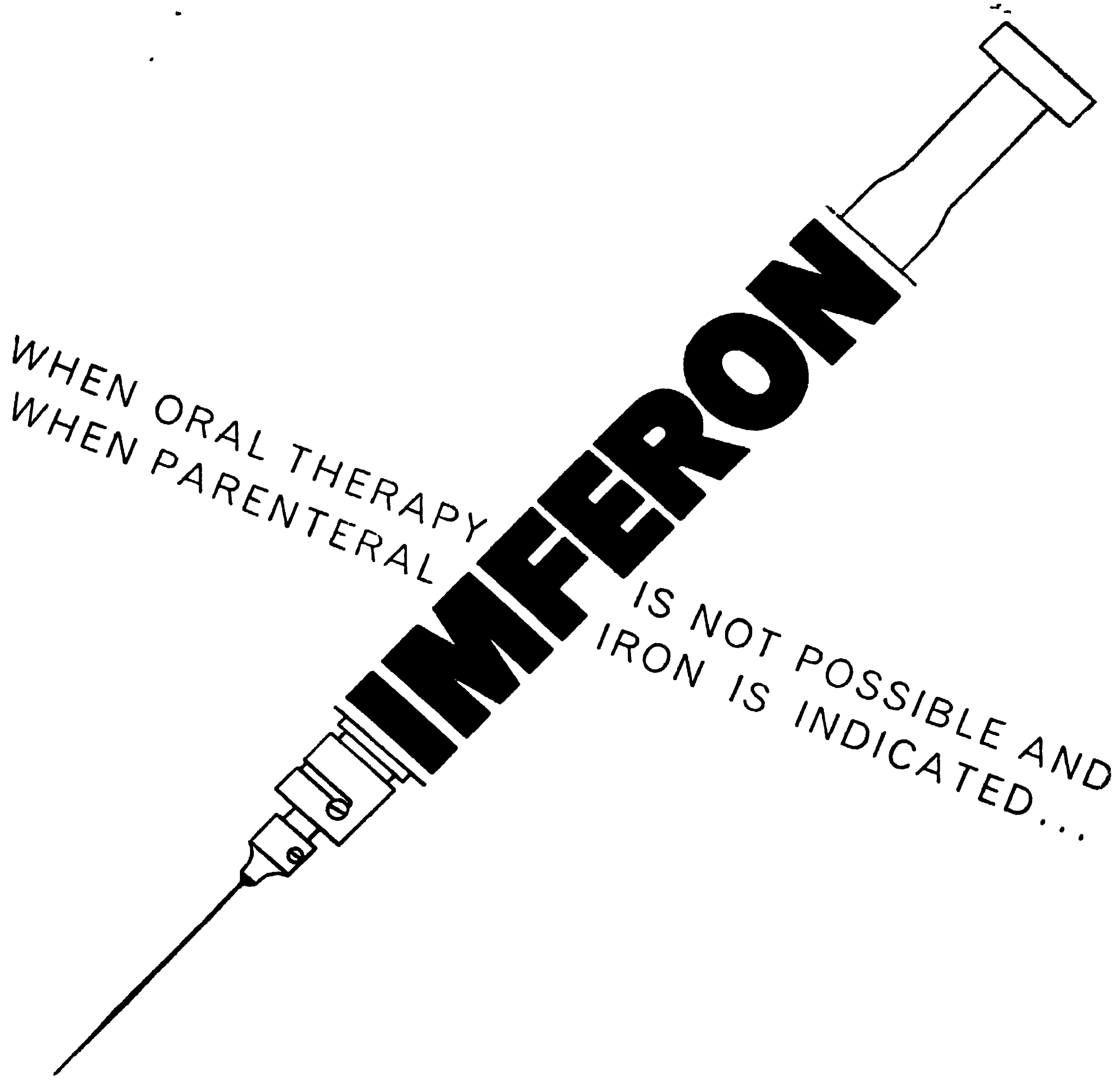

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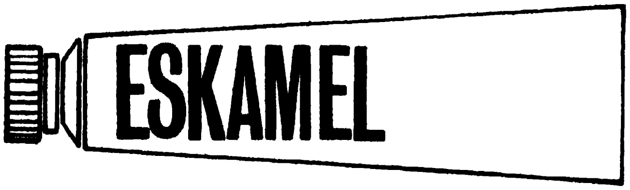

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1 W H O Chronicle Vol 16, March 1962, page 87
2. Goodman & Gilman 'The Pharmaco logical Basis of Therapeutics' page 1461, 1489 a
3. Foy (A) Kondi (A) J Trop Med. Hyg., 1957 60, 105.
4. Merck Manual page 245.

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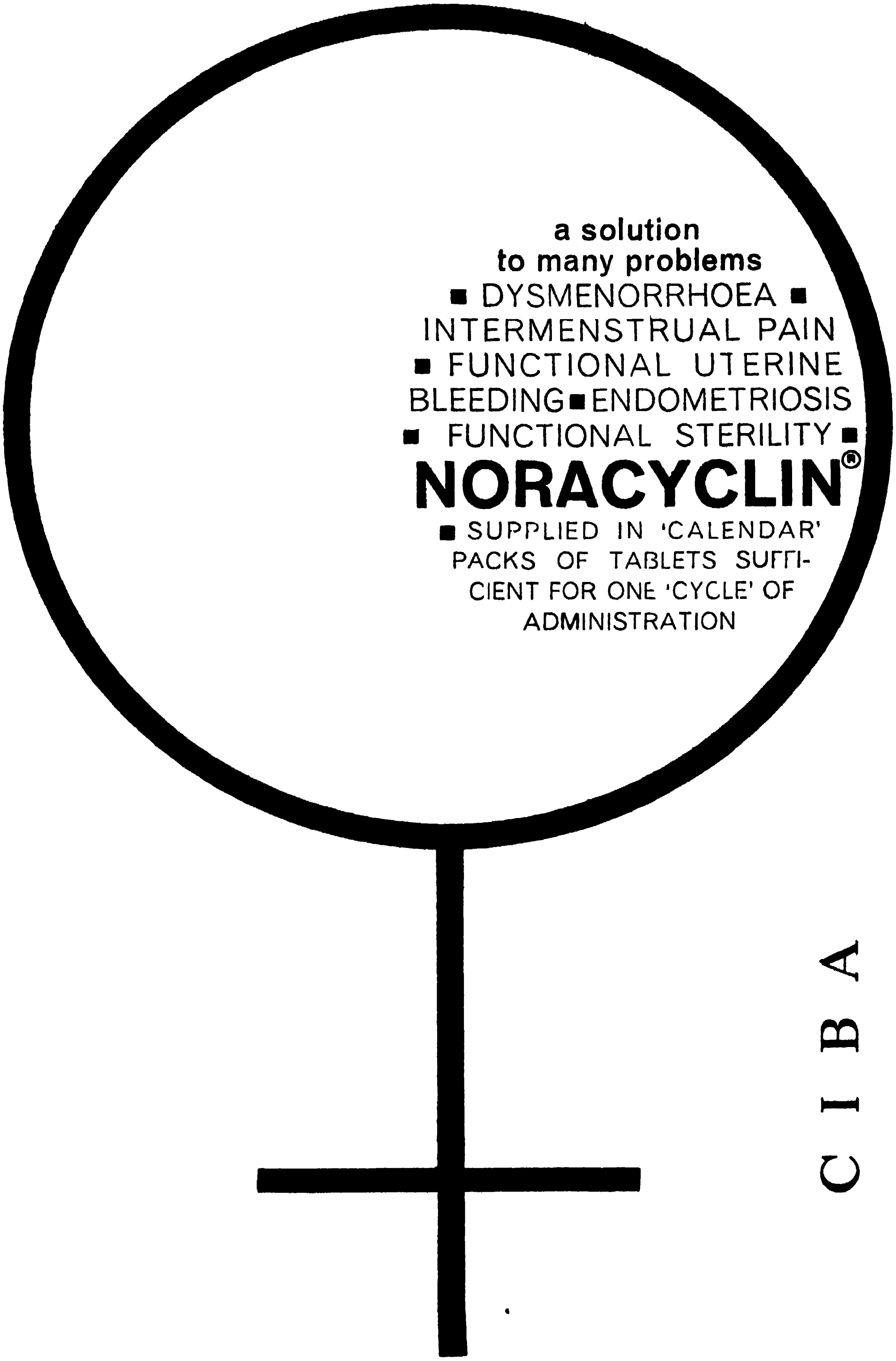

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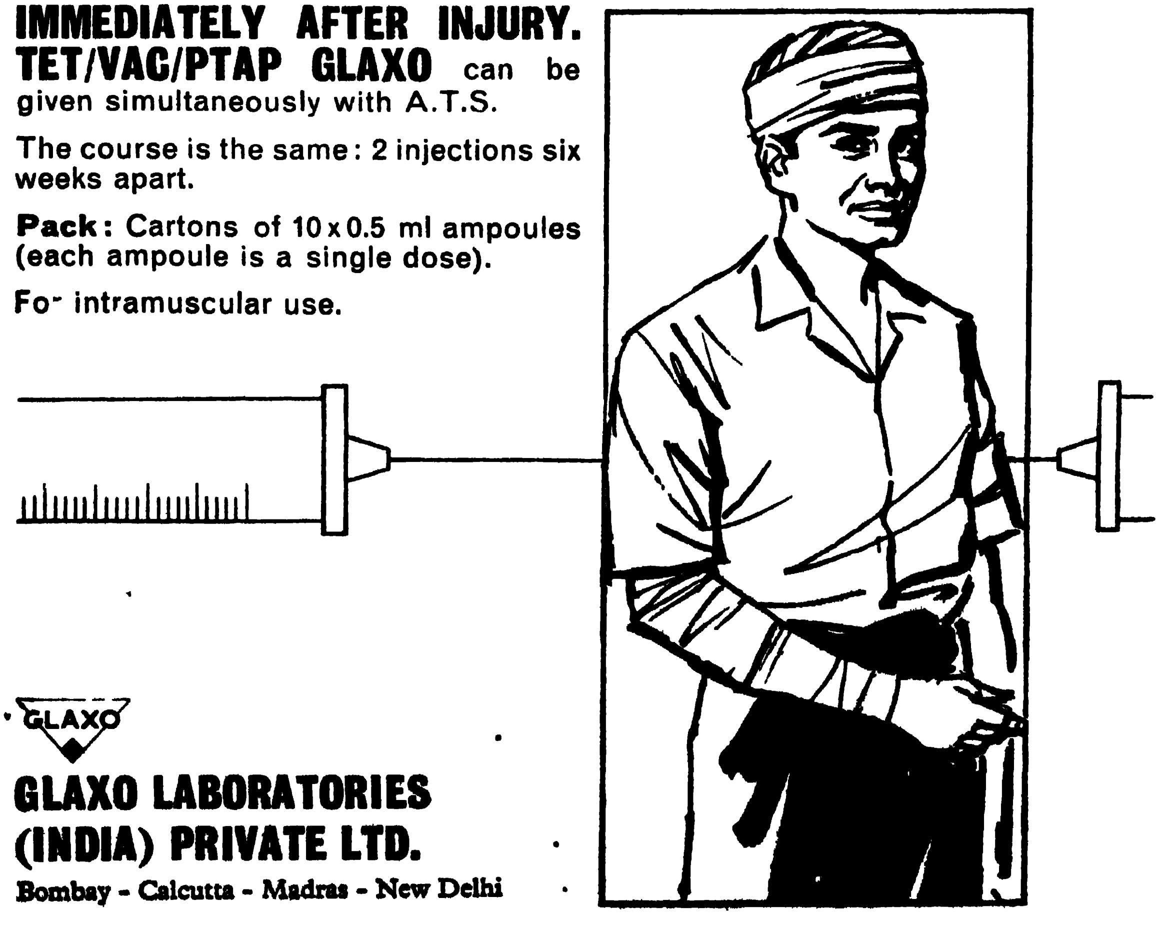

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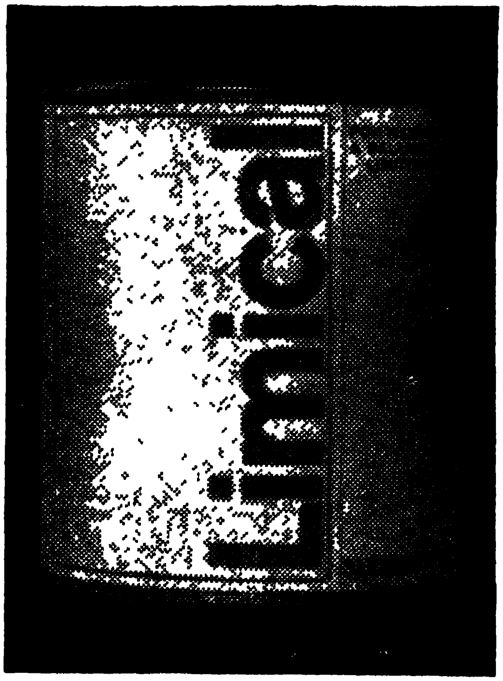

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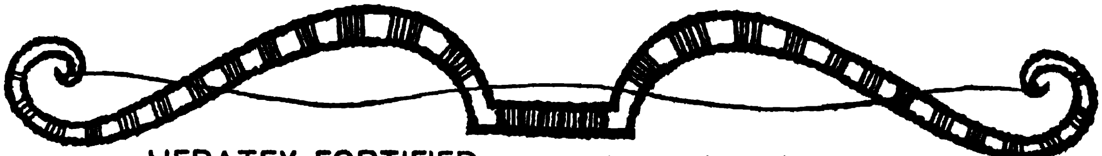

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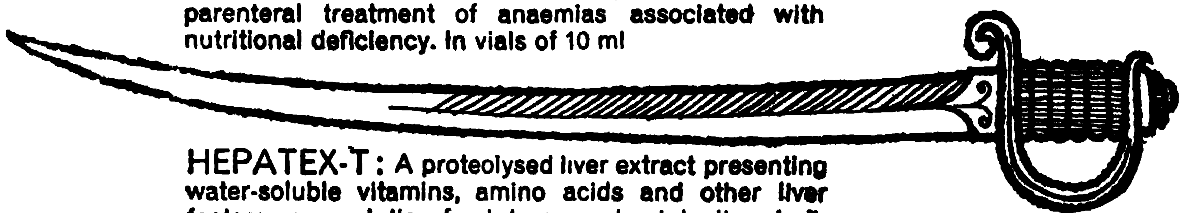

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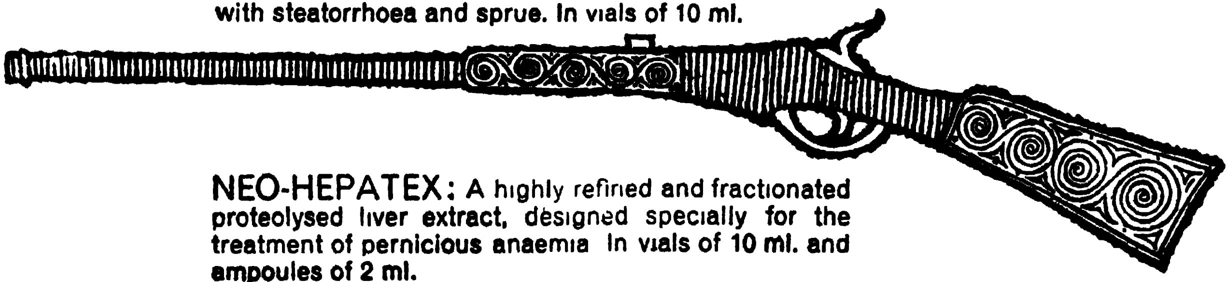

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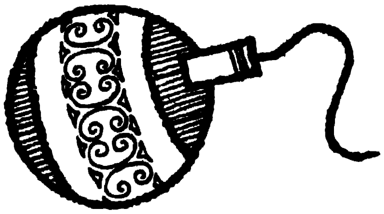

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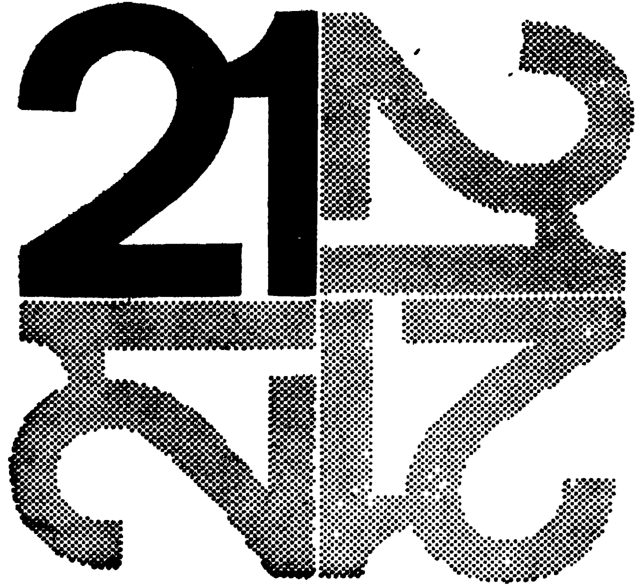

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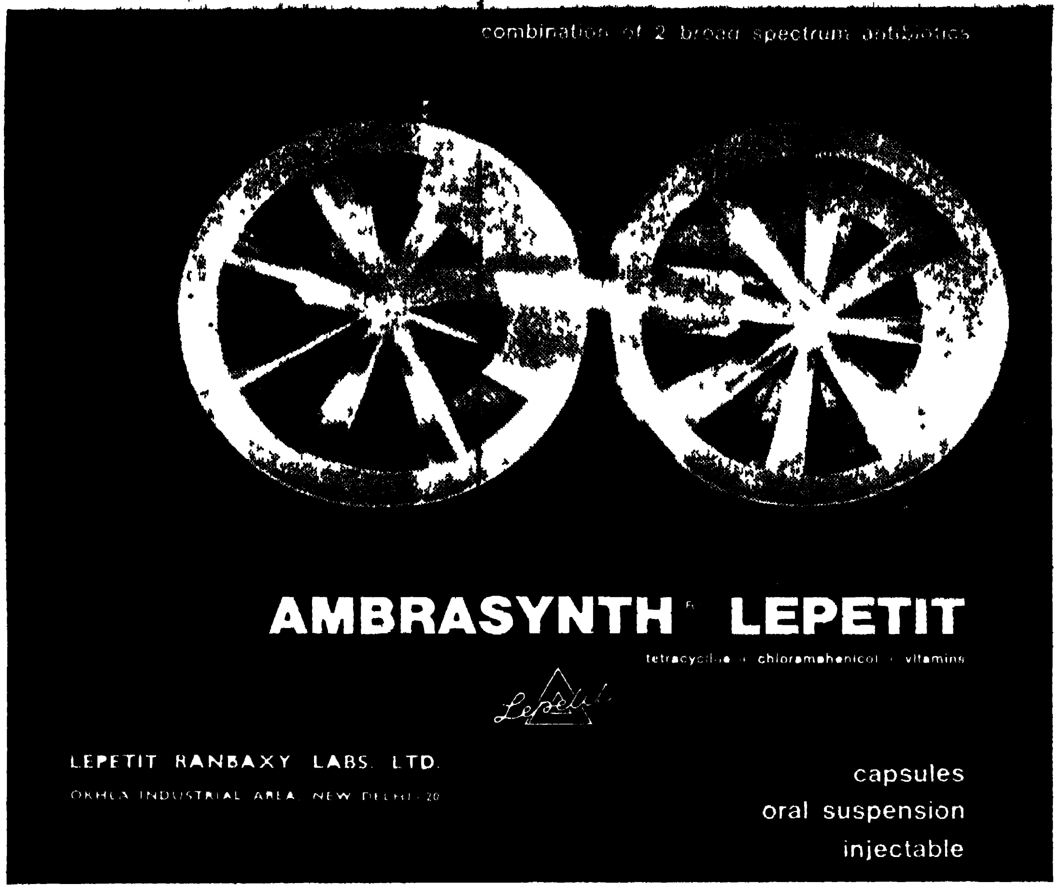

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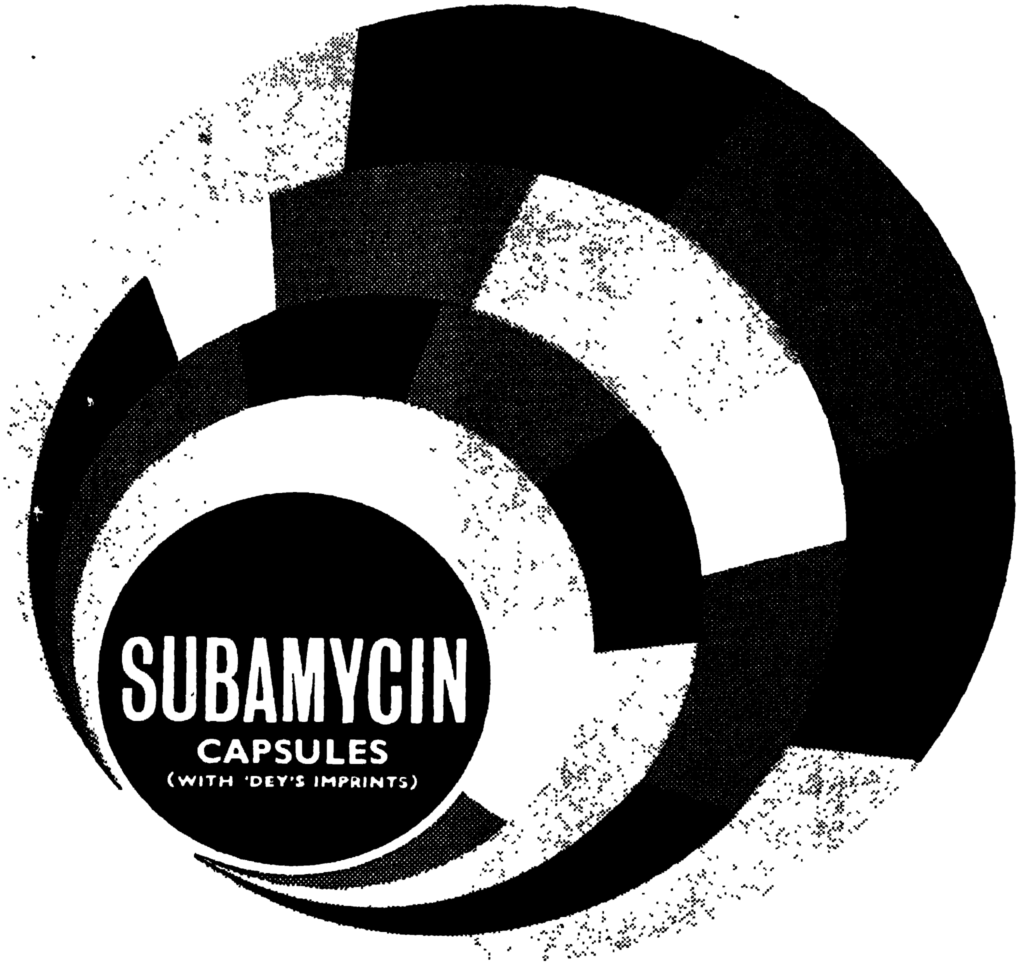

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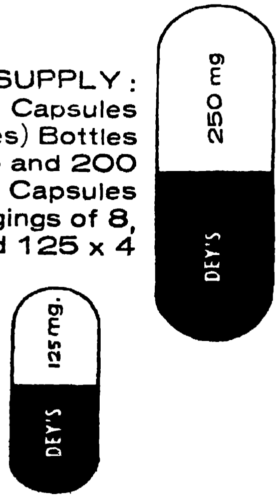

Journal of the Indian Medical Association

VOLUME 45
NUMBER 9

PUBLISHED TWICE A MONTH
EDITOR—N. BANERJEE, M.B. (CAL.), F.R.C.S. (ENG.), D.L.O. (LOND.)

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ORIGINAL ARTICLES

RADIATION NEPHRITIS IN MAN

L. P. DUTTA, M.B.B.S. (GAUHATI), PH.D. (SHEFFIELD)*

Department of Pathology, National Radiotherapy Centre, Sheffield, U.K.

Warthin in 1907 recorded mineral deposition in renal tubules and interstitial fibrosis of the kidney in two cases of myeloid leukaemia subjected to prolonged splenic x-irradiation. Domagk (1927) reported fatal nephropathy in a 9-year-old girl who was given a wrong dose of x-ray while being treated for mesenteric lymphadenitis. This is the first authentic report of a case of radiation nephritis. Since then several cases have been reported. The series of cases reported from the Holt Radium Institute, Manchester (Paterson, 1952 ; Russell, 1953), is the largest single series of cases reported in thorough detail. These authors have successfully painted a clear picture of radiation nephritis as a complication of abdominal irradiation. The literature on radiation nephritis has recently been reviewed (Redd, 1960 ; Heptinstall, 1960). The clinical and pathological features of all the histologically confirmed cases available in the literature are summarised in Table 1.

There are 36 confirmed cases of radiation nephritis available in the literature (Table 1). Thirty-three of these had hypertension as the main feature. There are reports of apparently cured cases, 5 after removal of the unilaterally affected kidney (Mertz *et al.* 1941 ; Dean and Abels, 1944 ; Levit and Oram, 1956 ; Cogan and Ritter, 1958 ; Rubenstone and Fitch, 1962) and 5 after institution of antihypertensive therapy (Cogan and Ritter, *loc. cit.* ; Jernigan, 1959, Rubenstone and Fitch, 1962). The mode of death in 25 fatal cases was as follows: uraemia (13), cerebral haemorrhage (3), heart failure (3), bleeding from the gut (2), pulmonary embolism (1) and intestinal obstruction (1). In 2 cases the mode of death was not clearly recorded. The aim of this paper is to report 6 more cases of radiation nephritis in man and to discuss the genesis of the main features of the syndrome.

CASE REPORTS

Case 1—D. F., age 36, male. On October, 1957 a laparotomy was performed with a suspected diagnosis of pericolic abscess. Large masses of nodes were found in the mesentery which were histologically diagnosed as lymphosarcoma. From November 26 to December 20 he received a total depth dose of 2500 r deep x-ray (DXR) to abdomen. During 1958 the patient further received some x-irradiation to mediastinum, neck and axilla. On 23-2-61 the patient was admitted with left ventricular failure and pneumonia. Examination revealed blood pressure 190/110 mm. Hg, blood urea 199 mg. per 100 ml. and hypertensive retinal changes. On 27-3-61 he developed cardiac asthma and blood urea started to rise gradually. On 6-4-61 he developed thrombophlebitis of right thigh. On 9-4-61 the patient died in uraemic coma. The post-mortem findings were : (1) lymphatic reticulosis, (2) left ventricular hypertrophy, (3) pulmonary oedema and (4) radiation nephritis.

Case 2—W. C., age 52, male. In May, 1952 a biopsy from a mass of nodes in the right groin confirmed lymphosarcoma. The patient received 13 courses of DXR at various sites for recurrent enlargement of lymph nodes. From 14-4-54 to 13-3-61 he received a total of 4600 r to the lumbar spine, spleen, abdomen and epigastrium and left loin, and the kidneys received a

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Table 1—Showing Summary of the Clinical Features of the Confirmed Cases of Radiation Nephritis from the Literature

Author (s)	No. of cases reported	Sex and age	Dose of x-ray	Symptoms	Latent period before symptoms	Follow-up
Domagk (1927) ...	1	F., 9 years	Massive	Albuminuria, uraemia	6 months	Died of uraemia after 6 months
Daube *et al.* (1927) ...	2	M., 45 „	...	Albuminuria, B. P. 195/106 mm.Hg	...	Not recorded
		F., 60 „	...	Albuminuria, B. P. 230/140 mm.Hg, blood urea 75 mg.%	10 „	Died of uraemia after 10 months
Mertz *et al.* (1941)	1	M., 29 months	16335 r	...	...	Nephrectomy — survived
Dean and Abels (1944) ...	1	F., 20 years	4600 r in 25 days	Hypertension, B. P. 184/125 mm.Hg	7 years	Nephrectomy — survived
Ritter and Scott (1949) ...	1	M., 10 „	6400 r within 7 months	Oedema, anaemia, B.P. 230/170 mm.Hg, blood urea 125 mg.%	8 months	Died of cerebral haemorrhage at 9 months
Zuelzer *et al.* (1950) ...	3	F., 4 „	5850 r in 5 months	Hypertension, anaemia, renal failure	7 „	Died of uraemia, after 7 months
		M., 3 „	5200 r in 5 months	Hypertension, ureamia, albuminuria, anaemia	7 „	Died of heart failure after 7 months
		M., 18 months	6850 r in 5 months	Hypertension, oedema, uraemia, albuminuria, anaemia	5 „	Died of uraemia after 6 months
Davey *et al.* (1952)	1	F., 40 years	4700 r	...	...	Died of cerebral haemorrhage
Russell (1953) ...	6	M., 32 „	2700 r in 37 days	Headache, oedema, albuminuria, B.P. 180/86 mm.Hg, blood urea 102 mg.%	9 months	Died of uraemia at 1 year
		M., 29 „	2700 r in 35 days	B.P. 170/100 mm.Hg, albuminuria, blood urea 105 mg.%, anaemia	1 year	Died of pulmonary oedema at 16 months
		M., 25 „	3000 r in 30 days	Dyspnoea, cardiomegaly, B.P. 190/95 mm.Hg, blood urea, 110 mg.%, anaemia, albuminuria	6 months	Died of uraemia at 9 months
		M., 46 „	2700 r in 25 days	B.P. 210/115 mm.Hg, blood urea 154 mg.%, albuminuria, anaemia	9 „	Died of uraemia at 13 months
		M., 33 „	1500 r in 8 days	No symptoms	5 weeks	Died of pulmonary embolism
		F., 45 „	2500 r in 30 days	B.P. 185/100 mm.Hg, albuminuria	5 months	Died at 8 months

TABLE 1—(*Contd.*)

Author (s)	No. of cases reported	Sex and age	Dose of x-ray	Symptoms	Latent period before symptoms	Follow-up
Grossman (1955)	1	M., 9 months	2000 r in 20 days	Oedema, B.P. 176/144 mm.Hg, anaemia, blood urea 92 mg.%	4 ,,	Died of cerebral haemorrhage at 6 months
Smith and Williams (1955) ...	1	M., 3 years	3300 r in 46 days	Oedema, B.P. 130/95 mm.Hg, blood urea 61 mg.%, albuminuria	2 months	Died of haematemesis and melaena at 4 months
Levitt and Oram (1956) ...	1	M., 33 ,,	2200 r	Headache, B.P. 215/130 mm. Hg	11 years	Nephrectomy—cured
Levitt (1957) ...	1	F., 31 ,,	3000 r in 49 days	Hypertension	10 months	Died of heart failure at 12 months
Cogan and Ritter (1958) ...	3	F., 49 ,,	1750 r in 51 days	Oedema, headache, B. P. 186/112 mm. Hg, albuminuria, anaemia	4 ,,	Antihypertensive treatment lowered B.P. to 150/90 mm.Hg
		F., 35 ,,	2000 r in 57 days	Headache, vomiting, B. P. 200/110 mm. Hg, anaemia, albuminuria	10 ,,	Treatment lowered B.P. to 130/80 mm. Hg
		M., 14 months	5300 r in 36 days	Irritability, vomiting, B. P. 150/100 mm. Hg, albuminuria	3 ,,	Nephrectomy—cured
Wilson *et al.* (1958) ...	2	F., 35 years	2000 r in 35 days	Vomiting, B.P. 190/115 mm. Hg	8 years	Died suddenly of uraemia
		M., 27 ,,	2000 r in 36 days	Breathlessness, dimness of vision, B.P. 210/130 mm. Hg, albuminuria	11 months	Died of uraemia at 11 months
Beck (1958) ...	1	F., 2½ ,,	3250 r to left 3000 r to right kidney in 28 days	Oedema, anaemia, B.P. 130/85 mm. Hg, blood urea 140 mg.%	4½ ,,	Died of uraemia at 4½ months
Schreiner and Greendyke (1959) ...	1	M., 11 months	4000 r in 26 days	Dyspnoea, melaena, retinal haemorrhage, B.P. 190/90 mm. Hg, blood urea 117 mg.%, albuminuria, anaemia	4 ,,	Died of uraemia at 8 months
Jernigan (1959)	1	F., 39 years	3000 r in 57 days	Dyspnoea, B.P. 210/120 mm. Hg—	10 ,,	Antihypertensive treatment stabilised blood pressure at 160/90 mm. Hg

TABLE 1—*Contd.*

Author (s)	No. of cases reported	Sex and age	Dose of x-ray	Symptoms	Latent period before symptoms	Follow-up
Rubenstone and Fitch (1962) ...	5	F., 33 ,,	2500 r in 60 days	Dyspnoea, oedema, B.P. 195/120 mm. Hg, blood urea 120 mg.%, anaemia, albuminuria	11 ,,	Antihypertensive treatment lowered B.P. to 160/90 mm. Hg
		M., 14 months	5300 r in 31 days	Irritability, vomiting, B.P. 150/100 mm. Hg, albuminuria	3 ,,	Nephrectomy lowered B.P. to 92/66 mm. Hg
Rubenstone and Fitch (1962)		F., 53 years	2500 r in 50 days	Oedema, anaemia, albuminuria, B. P. 210/100 mm. Hg	8 months	Died of intestinal obstruction 2½ years after
		F., 49 ,,	1750 r in 51 days	Oedema, headache, B. P. 180/112 mm. Hg, albuminuria	3 ,,	Antihypertensive regime stabilised B P. at 150-160/90-100 mm. Hg
		F., 35 ,,	2000 r in 59 days	Headache, vomiting, B.P. 200/110 mm. Hg, albuminuria	10 ,,	Antihypertensive treatment lowered B.P. to 140/84 mm. Hg, albuminuria persisted
Baldwin and Hagstrom (1962)	1	M., 63 ,,	3960 r in 39 days	Dyspnoea, headache, B. P. 230/120 mm. Hg, oedema, anaemia, blood urea 88 mg.%	5½ ,,	Died of uraemia after 9 months
Rosen *et al.* (1964)	2	F., 41 ,,	3000 r in 56 days	Oedema legs, dyspnoea, jaundice, pleural effusion, B. P. 210/110 mm. Hg, albuminuria, blood urea 220 mg.%	7 ,,	Died of uraemia after 9 months
		F., 2 ,,	4200 r in 6 months	Melaena	9 ,,	Died of bleeding from the gut after 9 months

large dose. The total depth doses applied to the spleen and left loin were 1000 r and 900 r respectively, which obviously affected the left kidney more than the right. On 31-8-61 the patient was admitted to hospital with dyspnoea and swollen legs. On 5-9-61 he died of cardiac failure. The post-mortem findings were: (1) lymphosarcoma, (2) pleural effusion, pericarditis and mediastinal fibrosis and (3) post-irradiation changes in the left kidney.

Case 3—F. R., age 44, male. In September, 1960 right orchidectomy was performed for a testicular tumour which was histologically diagnosed as a malignant teratoma without evidence of invasion. The patient had a course of soft x-ray of 4500 r depth dose to para-aortic and pelvic glands from 20-9-60 to 1-11-60. On 14-11-61 the patient was admitted as an emergency case with respiratory difficulty and left hemiplegia. Examination revealed complete V, IX and XI nerve palsy and blood pressure 180/120 mm. Hg. On 21-11-61 the patient died as a result of cerebral haemorrhage. The post-mortem findings were: (1) cerebral haemorrhage, (2) metastatic tumour, (3) post-irradiation renal changes, and (4) pulmonary embolism.

Case 4—S. B., age 20, male. In December, 1953 biopsy from painless enlarged supraclavicular glands established the diagnosis of Hodgkin's disease. Later,

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enlarged lymph nodes were found in several other sites and during the next 8 years he received 31 courses of irradiation from DXR and cobalt beam. This included a course of 1500 r depth dose to lower abdomen (12-1-56 to 3-2-56) and a course of 2000 r to right groin and 1250 to left groin (27-2-61 to 3-7-61). In November, 61 the patient developed swelling of the legs and genitalia and subsequently ascites. Examination revealed: blood pressure 165/80 mm. Hg, blood urea 184 mg. per 100 ml., and albuminuria. On 17-9-62 he developed signs and symptoms of uraemia (blood urea 200 mg. per 100 ml.) and died on 23-9-62. Post-mortem findings were: (1) acute necrosis of liver, (2) post-irradiation fibrosis in abdomen and mediastinum, (3) post-irradiation fibrosis of kidneys, (4) focal haemorrhage in the brain.

Case 5—S. R., age 42, male. In November, 1948 the diagnosis of Hodgkin's disease was histologically established. Since then on several occasions the patient had DXR therapy for enlarged glands. From 11-3-53 to 24-2-60 he received a total depth dose of 8750 r to abdomen and pelvis. On 24-7-62 he developed a cough, thirst and swelling of the legs. At that time his B.P. was 140/80 mm. Hg and blood urea 80 mg. per 100 ml. On 20-3-63 the patient was admitted to hospital with severe haematemesis, melaena, epistaxis and haemoptysis, and he died after two days with symptoms of uraemia (blood urea 456 mg. per 100 ml.). Post-mortem findings were: (1) pulmonary oedema, (2) uraemic pericarditis, and (3) radiation nephritis.

Case 6—R. W., age 40, male. On 10-5-60 his right inguinal hernia was repaired and right orchidectomy performed for a suspected testicular tumour. Histology revealed a seminoma of testis. From 15-5-60 to 29-7-60 a course of DXR of 3200 r depth dose was given to right abdomen. In December, 1962 the patient had a severe attack of epistaxis followed by occipital headache. Two months later his vision in the left eye became blurred. On examination: blood pressure 240/145 mm. Hg (previous records were 150/80 mm. Hg on 9-5-60, 190/30 mm. Hg on 13-11-62), hypertensive retinal changes and albuminuria were disclosed. Cystoscopy and intravenous pyelography showed a non-functioning right kidney. On 4-3-63 right nephrectomy was performed. Follow-up on 30-4-63 showed blood pressure subsiding to 145/95 mm. Hg.

COMMENT

Some degree of renal damage probably follows any therapeutic irradiation of the kidney region. Information so far accumulated shows that a total renal dose as low as 1750 r may initiate the kidney lesion, and that leads to clinical manifestation within a period of time varying from 2 months to 11 years. The syndrome consists of a variable degree of anaemia, albuminuria, hypertension and uraemia.

In the present series of 6 cases, 5 had hypertension and 4 had a high blood urea. Out of the 5 fatal cases, 3 died of uraemia, one with cerebral haemorrhage and one with cardiac failure. In the surviving patient, who had hypertension (240/145 mm. Hg), the blood pressure fell to 145/95 mm. Hg, 7 weeks after nephrectomy. The kidneys of these cases were subjected to histological and histochemical studies for acid mucopolysaccharides. The observations reveal tissue changes of progressive fibrosis of the renal parenchyma. This process has a special significance in the kidney.

Hypertension—It is known that ischaemia of the kidney produces hypertension. Such ischaemia may result from intrinsic fibrosis of the renal parenchyma. Involvement of only one kidney in such a process, for example, renal artery obstruction in man (Owen and Pearlman, 1952), unilateral radiation nephritis in man (Mertz, *et al.*, *loc. cit.*; Levitt and Oram, 1956) and the Case 6 in the present series, leads to sustained hypertension. In all these instances removal of the affected kidney has not only maintained normal renal function but has also significantly lowered the blood pressure. It indicates that like other conditions of renal hypertension, in radiation nephritis also the hypertension is the result of a reaction of some element of the renal tissue. The mechanism is not yet clearly understood.

Albuminuria—Albuminuria is a constant finding in florid cases of radiation nephritis. However, albuminuria is the sole finding in some cases where the kidney has been irradiated (Munger, 1937). Studies on 81 irradiated cases of Wilm's tumour and testicular tumours (Westfall, 1961) showed only albuminuria in 15 cases. Luxton (1961) in his report on a long-term observation from 5-19 years of a series of 54 patients recorded albuminuria only in 13 cases, and suggested that these patients seemed to have a latent nephritis. Renal biopsy studies, specially with the electron microscope, in these cases could be very interesting.

Uraemia—It is the commonest end result of radiation nephritis. Edsall and Pemberton (1907) observed nitrogen retention after x-irradiation in man. Several observers have confirmed this in experimental animals (Earlam and Bollinger, 1931). Usually in human cases of radiation nephritis, nitrogen retention follows hypertension and sooner or later chronic and progressive uraemia develops.

Anaemia—It is usually of normochromic type (Luxton, 1961) and is refractory to treatment. It is often confused with the haemolytic anaemia of chronic renal failure. However, the anaemia of uraemia is usually not so severe (Roscoe, 1952); and in many of these cases of radiation nephritis a severe progressive anaemia has been noted long before uraemia develops. Osnes (1959) after partial x-irradiation of the kidney and other experimental procedures in animals, showed that the kidney produces an important erythropoietic principle, apart from erythropoietin. He was of the opinion that the absence of this factor might be responsible for the anaemia of radiation nephritis.

From clinical and clinicopathological point of view radiation nephritis presents some intriguing features. For example, firstly, radiation nephritis bears a lot of resemblance to acute Bright's disease (Luxton, 1953) ; secondly, the pathogenesis of the refractory anaemia of radiation nephritis remains yet unexplained, and thirdly, the association of hypertension to the kidney lesions is still a riddle. It is obvious that much yet remains to be learnt about this problem. The proportion of patients that develop this syndrome, following therapeutic x-irradiation to the kidney area, has not been satisfactorily assessed. Clinical experience warrants a note of warning about radiation nephritis, but does not question the role of radiotherapy to the kidney region. A recent (Vaeth, 1964) follow-up report on 10 cases of Wilm's tumour treated with nephrectomy and post and preperative radiotherapy has shown no urological alteration in the remaining kidney up to 29 years after radiotherapy.

SUMMARY

Six cases of nephritis that developed after therapeutic irradiation over the renal area are reported. The clinical features of the histologically confirmed cases of radiation nephritis from the literature are analysed and presented in a tabular form. The genesis of the main features of clinical manifestation, namely, hypertension, albuminuria, uraemia and anaemia are briefly discussed. It is observed that the dose of abdominal irradiation that leads to this complication is a very variable one. The latent period before appearance of the symptoms and the rate of progress of the syndrome also varies enormously from case to case.

ACKNOWLEDGMENT

The author is grateful to the late Professor D. H. Collins, Professor of Pathology, The University, Sheffield, for encouragement during this study. Thanks are due to Mr. K. Sumner, Chief Administrative Officer, The United Sheffield Hospitals, for permission to publish the case records.

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EXPERIENCES WITH EXTRACORPOREAL CIRCULATION

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With the advent of extracorporeal circulation many intracardiac conditions and vascular problems can now be handled with success. The extracorporeal circulation is achieved through a very complex and precisely-built machine called 'Heart Lung Machine'. The present communication deals with the experiences and routine procedures that were practised at the Veterans Administration Hospital, West Roxbury, Massachussets, U.S.A., for patients undergoing surgery with the heart lung machine. No attempt has been made to discuss the merits of various types of heart lung machine now being used at the different cardiovascular centres.

A pump oxygenator built by Edward A. Olson Co. Ins., Ashland, Massachussets, is described in this article. This is principally a disc oxygenator of Key Cross type (Cross *et al.,* 1956) with roller DeBakey type occlusive pump.

DESCRIPTION OF THE PUMP

An ideal pump oxygenator is a unit that can temporarily take up the functions of the heart and the lungs efficiently during intracardiac or any bypass surgery without causing any damage to the vital organs and to the circulating blood and its system. The essential aspects of such a unit are that the different parts that will come in contact with the circulating blood can be sterilised easily and the surfaces shall be smooth, so that the blood does not stick during circulation.

The 'Olson's Heart Lung Machine' (Fig. 1), consists of a collecting system, rotating disc oxygenator, two roller pumps, filter and a bubble trap. A heating system is also incorporated in the unit to regulate the temperature of the blood to a desired level during work. All different parts of the unit are mounted and housed in a sturdy compact mobile unit.

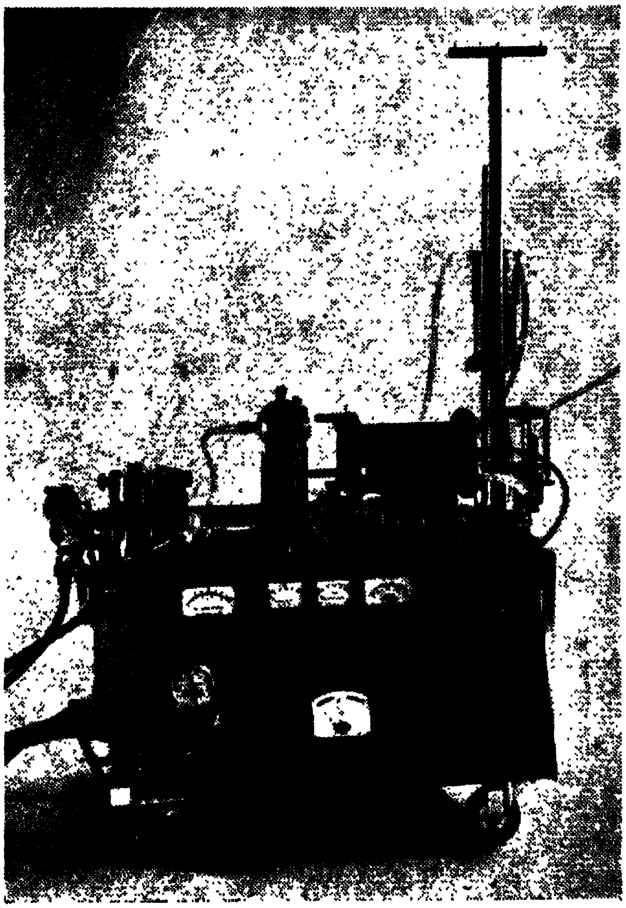


FIG. 1—SHOWING OLSON'S HEART LUNG MACHINE

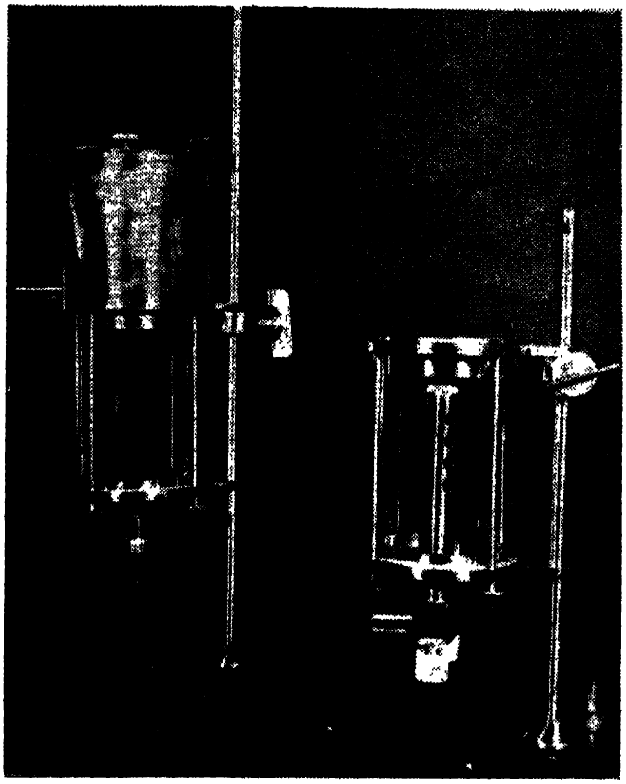


FIG. 2—SHOWING THE COLLECTING SYSTEM OF THE HEART LUNG MACHINE

The collecting system (Fig. 2) consists of two chambers, a collecting chamber and a settling chamber. They are constructed of graduated siliconised pyrex glass cylinders and stainless steel end plates. At the top of the collecting chamber, there are four stainless steel screens which are specially processed with silicon to defoam the blood that is sucked by the coronary suction system. The functions of the collecting system are to collect the caval blood and to drive the blood into the oxygenator after separating it from the intermixed air. The system is also used as reservoir during recirculation of the blood in the unit before the initiation of the bypass. All blood from the cavae is collected by two Bradic catheters connected through a stainless steel Y-connection to a Tygon tube (1/2 inch internal diameter) and allowing the blood to drain into the chamber by gravity. The collecting chamber can be adjusted at different levels to regulate the blood return. Blood from the cardiotomy wound is sucked away by the coronary suction system and is collected into the chamber after passing through the screens placed at the top of the chamber. In spite of this device, there is always some air bubbles intermixed with blood in this chamber. The intermixed blood is allowed to run through a Tygon tubing (5/8 inch internal diameter) on to the settling chamber. The blood is allowed to flow in this chamber through a vertical stainless steel tube with openings at the side. This arrangement allows the air bubbles to rise to the surface and the blood to flow from the collecting chamber to the settling chamber without any bubbles, a level of blood is always maintained in this chamber as a reserve blood for the oxygenator.

The oxygenator (Fig. 3) is, either 21 inch or 13 inch in length, of Key Cross type. The 21 inch oxygenator is used for adult patients and the 13 inch is used for children. The discs are flat stainless steel teflon coated and mounted on a horizontal shaft. Generally 118 discs are mounted with 0·140 inch spacing washer between them. The flow of blood to the oxygenator is from the bottom of the settling chamber through a right angle connection and 5/8 inch Tygon tubing to the end of the oxygenator. The blood level in the oxygenator is not allowed to rise over 1/3rd of the horizontal shaft. The oxygen flow to the chamber is maintained between 10 to 12 litres per minute from the oxygen tank through an oxygen flow meter mounted in the unit.

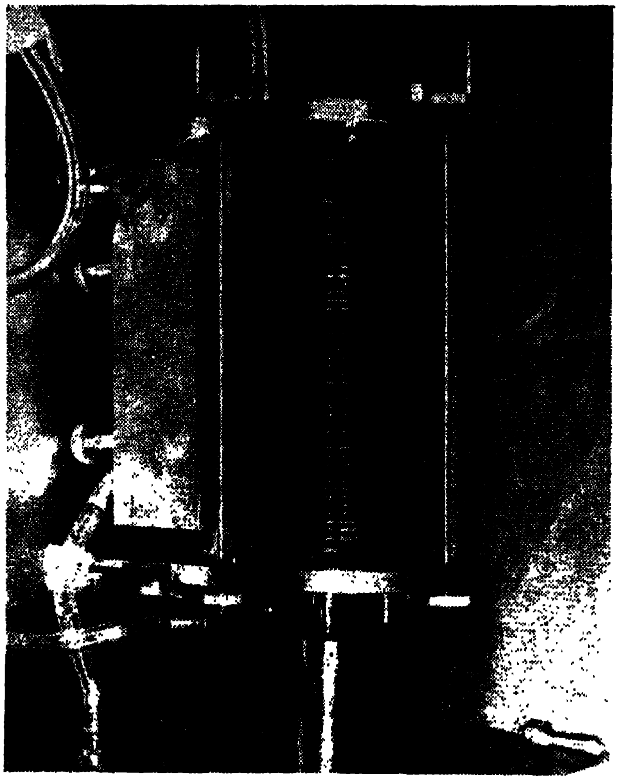


FIG. 3—SHOWING THE KEY-CROSS DISC TYPE (13") OXYGENATOR-RESERVOIR

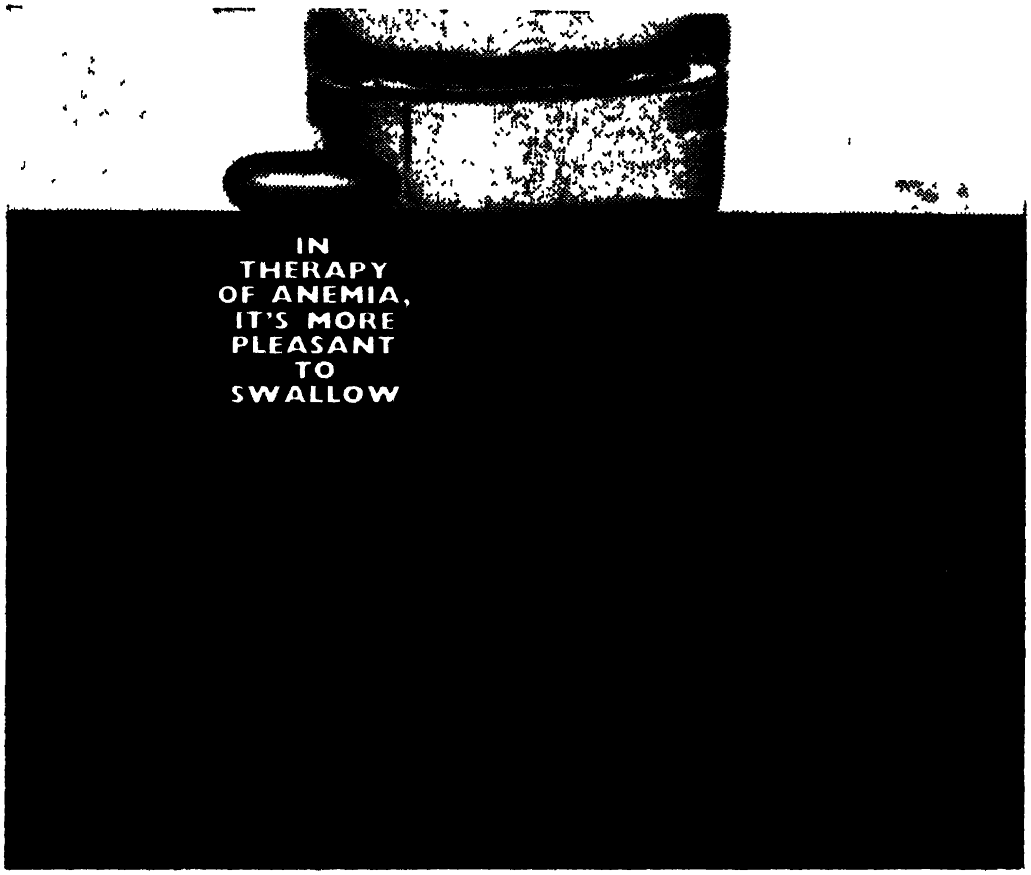
Pumps—The unit has two centrally adjusted rotary roller pumps of stainless steel, precisely built and engineered for the job with infinitely variable motor speed controls. Of the two pumps, one is for driving the blood from the oxygenator back to the patients and the other to suck away the blood from the cardiotomy wound to the collecting chamber. Tygon tubing (3/8 inch internal diameter) is used in this system. The large squeeze rollers are of stainless steel with ball bearing at the top and bottom, which are adjusted with a central graduated adjusting screw so that the pumps are set just off the occlusive. The coronary suction system has clamps for two tubes so that the two suckers can be used at the same time. The flow rate up to 5 litres per minute can be obtained against a pressure head of 150 mm. Hg.

Filter and bubble trap—This chamber is placed between the arterial pump and the patient. The blood from the arterial pump passes through a wire screen of 4½ inch diameter (a mesh of 20 wires per inch), placed vertically in the chamber, to the arterial line at the back of the filter. The entry and exit of blood is arranged in such a manner that any air in the chamber will rise at the top of the chamber. The air can be let out through a vent placed at the top of the chamber. The wire screen traps any fibrin during extracorporeal circulation.

Controls—There is a main switch for the complete unit ; however, each pump has its own separate motor, switch and circuit breaker, protecting against overload. The speed of the pump is controlled by a variac speed control for the oxygenator drive motor so that the oxygenator speed can be varied to control the amount of oxygen in the blood. Emergency cranks, for use in case of power failure, are mounted in an open box recessed into the rear of the cabinet. The cabinet is pressurised by a blower taking air from a stainless steel breather tube, which extends about five feet above the floor and pressurises the cabinet so that the explosive gases cannot collect in the unit.

Sterilisation—All tubings, all parts, chambers and oxygenator are sterilised by pressure autoclaving.

Temperature regulation system—Two main functions of this system are (i) to prevent any heat loss from the blood while circulating outside the body and (ii) to regulate the temperature of the blood according to the plan of operation.



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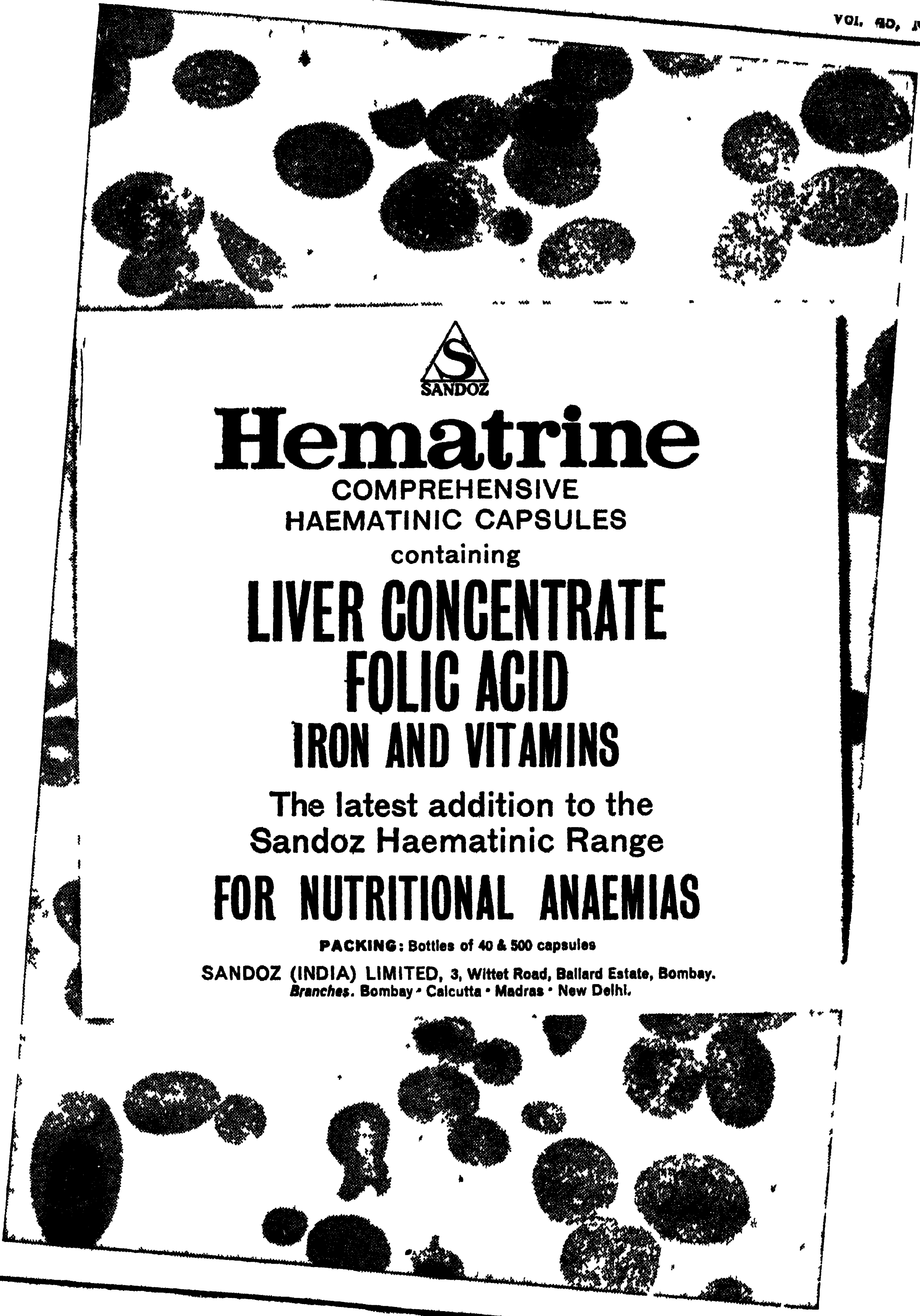

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A heat exchanger like Brown Harrison type is attached to the unit, through which blood is circulated before it is pumped back to the patient. The heat exchanger is raised vertically to eleminate any air in this part of the circuit and then repositioned. The mixing valve with recording gauze are mounted inside the cabinet. The hot and cold water from the unit are from the tap. The mixed water after being circulated in the heat exchanger is returned into a sink.

ROUTINE FOLLOWED AT THE VETERANS ADMINISTRATION HOSPITAL, WEST ROXBURY, MASSACHUSSETS, U.S.A., FOR OPEN HEART SURGERY

The candidate for open heart surgery is selected at the cardiac-surgical conference, where the history of illness and the cardiac catheterisation data are presented and discussed. The patient selected for surgery is then transferred to the surgical unit. The pulmonary function tests and haematological determinations are made prior to surgery. The preoperative and the postoperative administration of cardiac drugs are regulated by the medical colleagues.

Pump meeting—This is a conference held two days prior to surgery. All personnel directly or indirectly associated with the care of the patient at the time of surgery are requested to attend the meeting. The surgical resident in charge of the patient presents the history of illness. Table 1 represents the proforma of preoperative cardiac sheet. The surgeon describes the procedure of the operation that he is contemplating and assigns the responsibilities to different personnel attending the surgery. The physician in charge of the heart lung machine explains in details regarding the pump run, e.g., the temperature of the blood in the machine to be maintained during the procedure, the expected flow as calculated against the body surface area, amount of heparin to be injected to the patient, and the necessary amount of antiheparin drugs (polybrin of protamine sulphate) will be required to neutralise the heparin effect.

TABLE 1—SHOWING PROFORMA OF PREOPERATIVE SHEET FOR CARDIAC SURGERY

Name	Age	Sex	Case No.
Height	Weight	B.S.A.	
Diagnosis			
X-ray :			
R.A.	L.V.	Calcification	
R.V.	L.A.		
P.A.	Aorta		
Angiography :			
Cardiac Catheterisation Data :			
Pressures :			
R.A.	P.C.	Aorta	
R.V.	L.A.	Gradients	
P.A.	L.V.	Others	
E.C.G.			
Pulmonary Function Data :			
Drugs during last week (Digitalis, Quinidine)			
Laboratory Data :			
Electrolytes	Chemistry		
Clotting time	Platelets		
Liver function tests	Prothrombin		
Urine	Haematocrit		
	Blood volume		
Comments :			

Preparation of the pump—The different parts of the pump are assembled after proper sterilisation on the morning of the operation. The pump is primed with 3500 ml. of fresh heparinised blood, collected during past 24 hours of the operation. For hypothermic run, the procedure adopted was that the pump was primed with 3000 ml. of fresh heparinised blood and 500 ml. of low molecular dextran (rheomacrodex). The blood is recirculated in the machine slowly with the desired temperature using the heat exchanger. The function of recirculation is to drive out air from the arterial system and also to obtain an uniform temperature in the blood.

Temperature of the blood—During normothermic run it is maintained at 37·5° centigrade. Under this condition open mitral valvuloplasty and corrections of atrial septal defects are undertaken. Hypothermic condition is used for aortic valve surgery or any valve replacement surgery. The condition is obtained by bringing down the blood temperature to 10° centigrade at the initiation of the bypass and maintained till gross cardiac arrest is noticed. At this point the aorta is generally cross clamped and the blood temperature is raised up to 28° centigrade. This temperature of the blood is maintained throughout the procedure until the aortotomy wound is closed, when the temperature is raised up to 42° centigrade. Complete cardioplegia is obtained by packing the heart with normal saline ice slush placed in the pericardial pouch.

Technique of preparation of ice slush—Normal saline is poured in special metal jars (monel) fitted in a stainless steel box with sliding windows at the sides. The open windows facilitate for sterilisation of the contents of the box. The whole unit is then placed in an autoclave and sterilised at 250° Fahrenheit and 22 lb. pressure for 30 minutes. After sterilisation the open windows of the box are closed and the unit is transferred to a room with temperature —4° centigrade. The unit is kept there overnight. On the morning of the surgery the box is taken out and transferred to the operating room, where the solid ice from the jars is grinded with a sterile hammer.

Heparin—2·5 mg. per kilogram of the body weight is administered to the patient just prior to cannulation. In the priming blood the heparin content is 20 mg. per 500 ml. of blood.

Flow—The expected flow is calculated at the rate of 2·4 litres per minute per square metre of body surface area during normothermic run. The flow is determined indirectly during the run by temporarily occluding the Tygon tubing that connects the collecting chamber to the settling chamber for 5 seconds and measuring the blood level in the collecting chamber by means of a stationary vertical scale that has been calibrated from the known cross-sectional area of the chamber in such a way that the rising level of blood can be read directly from the scale in terms of cubic centimetre of blood.

Blood samples—At the cessation of the circulation the blood samples are taken either from the pump or from the patient to determine the arterial and venous oxygen saturation, free plasma haemoglobin and pH.

Neutralisation of heparin—The heparin effect is nutralised at the end of the bypass by adding to the blood 3·75 mg. of polybrin per kilogram of the body weight.

Recalcification time (Belko and Warren, 1958)—This test is done to ascertain the heparin effect that is left over in the blood after neutralisatoin. Blood from the patient is subjected to this test after 15 minutes of adding the antiheparin drug. The normal range of the test is considered between 5 to 8 minutes.

Cleaning of the pump—After the procedure the blood from the pump is drained out and the whole system is flushed with tap water and brushed with a soft mick pad. The parts are spread to dry on a clean sheet. Parts that need to such as threeway stop cocks are greased. The discs are spread to dry on layers of turkish bath towel side by side, so that no two surfaces are touching. This is important to prevent any scratching. After drying all the parts and discs, they are reassembled, and the machine is ready for further sterilisation.

METHOD OF EXTRACORPOREAL CIRCULATION

Generally two caval catheters, one in the superior vena cava and the other in the inferior vena cava, are introduced through purse string suture placed on the right atrium, for siphonage drainage. The catheters are held with umbilical tapes round the venae cavae. Sometime a single catheter (Bradic No. 40) is placed in the right atrium only for the venous drainage. The collected blood after being oxygenated in the oxygenator is returned to the body by an arterial cannula placed either into the left external illiac artery or into the left common femoral artery. Any kink or distortion in the line is checked before the initiation of the bypass. It is started by unclamping the caval line and simultaneously starting the arterial pump. The arterial flow is gradually increased, taking care to maintain the original blood level in the oxygenator, thus preventing a change in the patient's blood volume. The oxygen is flowed in the oxygenator at 10 to 12 litre per minute, after a few seconds following the initiation of the bypass in order to prevent high oxygen tension in the arterial blood. Complete bypass is achieved by tightening the umbilical tapes around the caval catheters. This increases the venous outflow. To achieve an ideal syphonage, the following points are to be considered :

1. Selection of proper catheters.
2. Exact positioning of the caval catheters, to prevent overlapping of the vessel wall onto the tip of the catheters.
3. Line must be free of any air.
4. A correct syphonage can be obtained by adjusting the height of the receiving chamber. It was noticed that the receiving chamber at 25 cm. below the venae cavae is the optimum position for the best syphonage.

During the initiation of the bypass the caval catheters should be checked separately. Sudden drop of venous flow indicates some mechanical obstruction or displacement of caval catheters, or loss of blood in the operating wound causing decrease in blood volume or pooling of blood in the viscera. A strict adherence to achieve the expected flow is not important as long as the systemic pressure is about 90 mm. Hg. Occasional checks on the perfusion rate are desirable. Intracardiac manipulation can be started when an adequate, stable and balanced rate of exchange of blood is achieved between the patient and the machine. The perfusion rate is increased if the blood level in the oxygenator rises above the original level. If it decreases with no venous hypotension, it indicates blood loss out of vascular system. Under such condition, extra blood is added into the oxygenator. Blood from the cardiotomy wound is sucked into the pump through the coronary suction system. Any other blood from the operating wound is sucked away by a separate sucker and is not returned into the system.

TABLE 2—SHOWING AVERAGE PERFUSION DATA OF 28 PATIENTS UNDERGOING SURGERY WITH DISC OXYGENATOR

No. of patients	Body surface area (m²)	Flow rate ml./min.	O_2 saturation		Arterio-venous O_2 difference	pH	Free plasma Hb. mg./100 ml.	Recalcification time (min.)
			Arterial	Venous				
24 patients with perfusion more than 60 minutes	1·83	3316	95·6	73·19	22·41	7·49	123	5
4 patients with perfusion more than 60 minutes	1·87	3200	97·07	65·7	31·37	7·52	79	4·5

TABLE 3—SHOWING DATA OF 28 PATIENTS UNDERGOING COMPLETE BYPASS

Type of cases	No. of patients	Average body surface area (m²)	Average perfusion period (min.)	Average flow rate (ml./min.)	Results		
					Alive	Operative death	Hospital death
Atrial septal defects	5	1·82	46	3260	4	nil	1
Mitral stenosis	1	1·68	46	2800	nil	nil	1
Mitral regurgitation	1	1·82	121	3100	1	nil	nil
Aortic stenosis with mitral stenosis ...	1	1·6	83	3400	1	nil	nil
Aortic stenosis	10	1·83	105	3210	6	1	3
Aortic incompetence	9	1·98	110	3050	4	2	3
Aneurysm of ascending aorta	1	1·7	113	3000	nil	nil	1

CLINICAL EXPERIENCE

The perfusion data of 28 patients undergoing surgery with the described heart lung machine, are presented in Table 2. Twenty-four patients were on bypass for more than 60 minutes. The average perfusion rate was maintained well over 3000 ml. per minute. At the end of the perfusion the pH was within normal level. The average free plasma haemoglobin was 123 mg. in group subjected to bypass for more than 60 minutes. This may be considered to be a little on the higher side, but none of the patients showed any untoward effects due to this. The average A-V oxygen difference in both groups was within normal limits at the end of the perfusion. Table 3 represents the various types of cases treated surgically under complete bypass. Hospital death was considered, if the patient died after some days of the procedure, and the operative death when the patient died either at the operating table or during immediate postoperative period. Table 4 represents the average perfusion data of 22 patients undergoing complete bypass under hypothermic condition. The perfusion rate was maintained well over 3000 ml. per minute. The A-V oxygen difference was also within normal limits. The pH was almost normal.

TABLE 4—SHOWING DATA OF 22 PATIENTS UNDERGOING COMPLETE BYPASS UNDER HYPOTHERMIC CONDITION

No. of patients	Body surface area (m²)	Average perfusion period (min.)	O_2 saturation		Arteriovenous O_2 difference	pH	Free plasma Hb. mg./100 ml.	Recalcification time (min.)
			Arterial	Venous				
22	1·86	110	97·5	70·69	26·82	7·48	109·7	4·79

Types of cases: Aortic stenosis—10; Aortic incompetence—9; Mitral regurgitation—1; Aortic stenosis with mitral stenosis—1; Aneurysm of the ascending aorta—1.

DISCUSSION

Various types of oxygenator are used at different open heart centres, such as the helix reservoir bubble oxygenator of DeWall and Lellihei, vertical screen oxygenator as used in Mayo Clinic and the reservoir type rotating disc oxygenator of Key-Cross, are few to be mentioned. The adaptability of the oxygenator depends on the condition and the experience of the personnel of the institution than those of another. We have used the bubble oxygenator (Foreggor Pump) but ultimately abandoned it because of various problems encountered during prolonged perfusion. We are, however, satisfied with our present pump with reservoir type Key-Cross oxygenator. Our mortality is comparatively higher, and this can be attributed to our selection of patients from the veterans with chronic illness of long standing and because of a higher age group, i.e., over 45 years of age, and last of all our very limited experience with the replacement cardiac surgery. No single mortality in the present series can be attributed to be due to mechanical inefficiency. However, we feel confident that our mortality rate will improve with more experience.

SUMMARY

The preoperative routine for cardiac patients selected for open heart surgery at the Veterans Administration Hospital, West Roxbury, Massachussets, U.S.A., is described.

The different parts of 'Olson's Heart Lung Machine' with Key-Cross type rotating disc oxygenator are described. The system runs as follows: Caval blood from the patient collected by two caval catheters is siphoned into the oxygenator, is pumped back to the patient *via* external iliac artery or common femoral artery.

The post-operative care and maintenance of the pump have been outlined.

The results of 28 patients, of which 22 were under hypothermic condition, have been discussed. The blood chemistry was noted to be normal at the cessation of the bypass. A slight rise of free plasma haemoglobin was noticed in those patients, who underwent bypass for more than 60 minutes.

ACKNOWLEDGMENT

I am thankful to Dr. Richard Warren, Clinical Professor of Surgery, Harvard Medical School, Chief of Cardiovascular Surgery, Veterans Administration Hospital, West Roxbury, Massachusetts, U.S.A., for allowing me to publish this paper.

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BRONCHIAL ASTHMA AND CHRONIC BRONCHITIS

A Pilot Survey

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Data regarding incidence of bronchial asthma in India are meagre. As it is the case with any other disease, morbidity rate in regard to asthma can only be estimated, for obvious reasons, by random surveys in different parts of the country. In order to find out the feasibility of such surveys, a pilot asthma survey was recently conducted by us at the Rajendra Memorial Research Institute of Medical Sciences in and around Patna so as to cover both urban and rural population groups.

As representative of the rural population, the village Pahari near Agamkuan was selected while for representing the urban population ward No. 19 of Patna Municipal Corporation near the City Court was chosen. All the people living in the areas selected were included in the survey. The number in the rural group was 920 including men, women and children of all ages. The urban group included 1000 people.

A special questionnaire was prepared and answers to questions were entered in the proforma, in respect of every one of the population surveyed. Those who had respiratory symptoms were examined then and there by one of us to exclude all organic lung diseases. They were also requested to go to the Institute for further investigations and treatment. More than 50 per cent of those who had symptoms availed of the facilities provided at the Institute.

Since the proforma included questions not only in regard to bronchial asthma but also to chronic bronchitis and smoking habits, useful data were obtained in respect of all the three conditions.

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The data were collated and statistically analysed by one of us (S.S.P.) and the results obtained are given below.

RESULTS

The age and sex distribution of the total population surveyed in urban and rural areas are given in Table 1.

TABLE 1—SHOWING AGE AND SEX INCIDENCE

Age group (years)	No. surveyed Male	No. surveyed Female	Total
0—9	287	235	522
10—29	433	292	725
30—49	226	192	418
50—69	120	94	214
70 & above ...	27	14	41
Total	1095	827	1920

Table 2 gives the sex-wise distribution of the prevalence of bronchial asthma in rural and urban areas surveyed.

TABLE 2—SHOWING SEX-WISE DISTRIBUTION OF THE PREVALENCE OF BRONCHIAL ASTHMA IN RURAL AND URBAN AREAS SURVEYED

	Rural Male	Rural Female	Rural Total	Urban Male	Urban Female	Urban Total
Asthmatics ...	14	11	25	6	10	16
Non-asthmatics ...	524	371	895	549	435	984
Total	538	382	920	555	445	1000
		$\chi^2 = 0{\cdot}0649$ p 0·75 Insignificant			$\chi^2 - 2{\cdot}1331$ p 0·10 Insignificant	

It will be seen from Table 2 that there is no significant difference in the incidence in the urban and rural population nor is the difference in regard to sex incidence statistically significant.

The age distribution and prevalence of bronchial asthma in rural and urban areas surveyed are given in Table 3.

It will be seen from Table 3 that the incidence of asthma is higher in the higher age groups. Such increasing incidence with age is found both in the rural and urban areas.

TABLE 3—SHOWING AGE DISTRIBUTION AND PREVALENCE OF BRONCHIAL ASTHMA IN RURAL AND URBAN AREAS SURVEYED

Age (years)	Rural No. surveyed	Rural No. of asthmatics	Urban No. surveyed	Urban No. of asthmatics
0—9 ...	236	0 (0%)	286	1 (0·35%)
10—29 ...	351	5 (1·4%)	374	2 (0·53%)
30—49 ...	205	9 (4·4%)	213	10 (4·69%)
50—69 ...	106	9 (8·5%)	108	1 (0·93%)
70 & above ...	22	2 (9·1%)	19	2 (10·52%)
Total ...	920	25 (2·7%)	1000	16 (1·6%)

Information was obtained from the questionnaire in regard to certain allergic factors. It was found that 2 persons were allergic to certain articles of food, 13 to dust, 2 to bad smell and 6 to both food and dust. The remaining 18 did not give any definite allergic history.

TABLE 4—SHOWING DISTRIBUTION OF ALLERGIC FACTORS IN THE BRONCHIAL ASTHMA CASES (RURAL AND URBAN)

Allergic factors	No. of cases
Food only	2 (4·9%)
Dust only	13 (31·7%)
Smell only	2 (4·9%)
Food and dust	6 (14·6%)
No allergy	18 (43·9%)
Total	41 (100%)

In order to determine the role of heredity in bronchial asthma the information obtained regarding family history was analysed for the whole population surveyed, both urban and rural, for finding out how many amongst asthmatics had positive history of asthma amongst the members of their families and how many amongst the non-asthmatics gave similar history. The data obtained are given in Table 5.

TABLE 5—SHOWING THE INCIDENCE OF FAMILY HISTORY OF BRONCHIAL ASTHMA IN THE POOLED SAMPLE .

Family history	Present	Absent	Total
Asthmatics . .	14 (34·1%)	27 (65·9%)	41 (100%)
Non-asthmatics ...	307 (16·3%)	1572 (83·7%)	1879 (100%)
Total ...	321	1599	1920

$\chi^2 = 8{\cdot}64$; 0·01 p 0·05 Significant.

It will be seen from Table 5 that whereas 34·1 per cent of asthmatics had positive hereditary history only 16·3 per cent of the non-asthmatics gave similar history. The difference has been found to be statistically significant.

Out of 41 persons who had bronchial asthma 17 had attacks throughout the year, 22 during winter, one during the rainy season and one during the change of season. In 17 the attacks were reported to occur during night, in 3 during the early morning, in 10 during the day and in the remaining 11 during any part of day or night. The percentage distribution of the above mentioned data are given in Table 6.

TABLE 6—SHOWING DISTRIBUTION OF THE TIME OF OCCURRENCE OF THE ATTACKS IN THE DAY AND IN THE YEAR

Season	No. of cases	Time of the day	No. of cases
Perennial ...	17 (41·5%)	Night ...	17 (41·5%)
Winter only ...	22 (53·7%)	Early morning ...	3 (7·3%)
Rains only ...	1 (2·4%)	Day only ...	10 (24·4%)
Change of season ...	1 (2·4%)	Any time ..	11 (26·8%)
Total ...	41 (100%)	Total ...	41 (100%)

Since information regarding smoking habits was obtained from all the persons included in the survey, the data were analysed to find out the possible correlation between asthma and smoking. It was found that whereas 17 (41·4 per cent) out of 41 asthmatics were smokers, only 351 (18·7 per cent) out of 1879 among the non-asthmatics indulged in smoking. Statistical analysis showed that the difference was highly significant (Table 7).

TABLE 7—SHOWING CORRELATION BETWEEN SMOKING AND BRONCHIAL ASTHMA

	Smokers	Non-smokers	Total
Asthmatics ...	17 (41·4%)	24	41
Non-asthmatics ...	351 (18·7%)	1528	1879
Total ...	368	1552	1920

χ^2 = 13·45 ; p 0·01 Highly significant.

Amongst the population surveyed 32 persons conformed to the diagnosis of chronic bronchitis as judged by symptoms and physical signs. 18 were males and 14 females (Table 8).

TABLE 8—SHOWING PREVALENCE OF CHRONIC BRONCHITIS SEX-WISE

	Male	Female	Total
Bronchitics ...	18	14	32
Non-bronchitics ...	1075	813	1888
Total	1093	827	1920

χ^2 = 0·006 ; p 0·80 Insignificant.

Table 9 gives the age distribution for chronic bronchitis. Just as in asthma, the incidence of chronic bronchitis is higher in the higher age groups.

TABLE 9—SHOWING AGE DISTRIBUTION OF CHRONIC BRONCHITICS

Age (years)	Total surveyed	No. of bronchitics
0—9	522	2 (0·38%)
10—29	725	5 (0·69%)
30—49	418	11 (2·63%)
50—69	214	5 (2·34%)
70 & above ...	41	5 (12·20%)
Total ...	1920	32 (1·67%)

20 (62·5 per cent) out of 32 chronic bronchitics were smokers whereas among the remaining 1888 normal persons only 348 (18·4 per cent) smoked. The difference in regard to the smoking habits between the bronchitics and non-bronchitics is highly significant as will be seen in Table 10.

TABLE 10—SHOWING CORRELATION BETWEEN SMOKING AND CHRONIC BRONCHITIS

	Smokers	Non-smokers	Total
Bronchitics ...	20	12	32
Non-bronchitics ...	348	1540	1888
Total	368	1552	1920

χ^2 = 39·11 ; p 0·001 Highly significant.

DISCUSSION

The information obtained from the present pilot survey has brought out some interesting facts regarding the incidence of asthma and chronic bronchitis, and their relationship to smoking habits.

The incidence of asthma in the rural and urban areas works out to 2·7 per cent and 1·6 per cent respectively. The difference in the incidence is not very significant. There is no significant difference in the sex incidence of the disease. It is of interest, however, to note that the incidence of the disease is higher in the higher age groups. The morbidity survey conducted amongst the Central Government servants and their families in Delhi in 1961 provided more or less the same results regarding the age incidence of asthma. It was found in that survey that whereas the incidence during the first year of life was 0·26 per cent it rose to 6·6 per cent in the age group 60 and above. In the present survey the incidence was 0·15 per cent in the age group 0-9 whereas it was 10·2 per cent in the age group of 70 and above in the urban population. Somewhat similar figures were also obtained for the rural population. The age specific incidence found in the present survey is not in consonance with the general impression that bronchial asthma is more common in children than in other age groups. Such impressions are gathered both in hospital and general practice because of the fact that parents seek medical aid more readily for the children than for themselves. Moreover, asthma is generally considered incurable and as such adults do not ordinarily go to a doctor or to a hospital except when they are severely incapacitated. Hardie (1965), the President of the Asthma Foundation of New South Wales, Australia, has made similar observations regarding his own country. Such a situation provides additional argument for the need to conduct epidemiological surveys for determining the actual incidence of disease.

Another interesting observation that has been made during the present survey is that there seems to be significant correlation between asthma and smoking. We do not propose to draw any conclusion regarding this correlation unless it is confirmed by large-scale surveys.

Analysis of data regarding hereditary factor in asthma has confirmed the previous observations made by Viswanathan (1962). In the present survey, hereditary history of asthma is significantly more common is asthmatics than in non-asthmatics.

The incidence of chronic bronchitis in the total population surveyed works out to 1·6 per cent. In a survey conducted by Viswanathan (1964) among Delhi University employees the incidence of chronic bronchitis was found to be 6 per cent. Wig *et al.* (1964) found an incidence of 3 per cent in a rural area near Delhi and 1 per cent in an urban area in Delhi for chronic bronchitis. Variations in the different surveys can be accounted for by the smallness of the group surveyed. It is, however, clear that chronic bronchitis affects more than 1 per cent of the population. Only by large-scale surveys can it be possible to find out the exact incidence of the disease in different regions in this country.

There is a highly significant correlation between smoking and incidence of chronic bronchitis in the present survey. This only confirms the observations made by other workers.

SUMMARY

A pilot epidemiological survey to determine the incidence of chronic bronchitis and asthma was conducted in rural and urban population in and around Patna city.

The incidence of bronchial asthma in the rural and urban areas was found to be 2·7 per cent and 1·6 per cent respectively.

The incidence of asthma is found to be higher in higher age groups.

Heredity plays a significant part in the incidence of asthma.

There appears to be significant correlation between smoking habits and asthma.

1·67 per cent of the total population surveyed, urban and rural, conformed to the diagnosis of chronic bronchitis.

There is a significant correlation between smoking habits and incidence of chronic bronchitis.

Larger epidemiological surveys to determine the incidence of different respiratory diseases in India are warranted.

ACKNOWLEDGMENT

Our grateful thanks are due to Dr. P. N. Sinha, Secretary, Rajendra Memorial Research Society for Medical Sciences, and Dr. Madan Prasad, Director and Professor of Pathology, Rajendra Memorial Research Institute of Medical Sciences, Patna, for their assistance in conducting the survey.

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OBSERVATIONS ON ENCEPHALITIS IN CHILDREN AT BHOPAL

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Though epidemics of encephalitis have visited mankind since the 17th century in different parts of the world, the first classical description in the literature was by von Economo in 1917. Encephalitis as a clinical syndrome has been accepted, although the mystery about the aetiological agent still remains unsolved.

Encephalitis generally connotes inflammation of the brain substance by microbes, viruses or toxins. It occurs sporadically or in epidemic form. Allergic brain tissue reaction should not be lost sight of in considering these epidemics, as demyelination has been known to occur due to brain tissue allergy. Leptospirosis may produce the same type of clinical picture with or without jaundice. Neurotropic viruses are known to be causative of some cases of encephalitis. Viruses may be transmitted by mosquitoes, ticks or by infected food directly or indirectly, the channels of infection being ingestion, inhalation or injection.

Encephalitis lethargica, equine encephalitis, inclusion body encephalitis, swine herds encephalitis, Japanese B encephalitis, St. Louis encephalitis, West Nile viruses encephalitis, Australian X fever, viral encephalomyocarditis and Russian spring-summer encephalitis and louping ill encephalitis due to viruses of herpes simplex, herpes zoster, mumps, measles, chickenpox, smallpox, benign lymphocytic choriomeningitis, coxsackie group and acute haemorrhagic leuco-encephalitis, benign myalgic encephalitis and polioencephalitis are known. It is very necessary that a correct clinical diagnosis be made as otherwise a wrong diagnosis may mean an unnecessary panic.

Encephalitis, its aetiology, epidemiological features, diagnosis and prevention all present problems which baffle the physician of today, but remain to be solved some day by modern medicine through organised medical research in the field.

MATERIAL AND METHOD

The material in this study comprised of 38 cases of encephalitis diagnosed clinically and admitted between June 1961 and February 1963 in the paediatric ward of Hamidia Hospital, attached to Gandhi Medical College, Bhopal. Majority of the patients belonged to the middle and low social strata of the population which paralleled the general admission pattern in the paediatric ward.

Only those cases were included which showed some sign of encephalon involvement by way of abrupt onset, irritability, variable degree of loss of consciousness from drowsiness to coma, twitching of facial and limb muscles, involuntary bizarre movements of limbs, rigidity or flaccidity of muscles, changes in pupils, conjugate deviation of eyes, paralytic and extrapyramidal neurological features in association with pyrexia, toxaemia and vomiting. Moreover, in these cases no other diagnostic label was possible even after cerebrospinal fluid examination and observation of the clinical progression of the disease. Blood examinations for total and differential leucocyte counts and stool examination for worm infestation were done wherever possible.

OBSERVATIONS

The observations made on 38 children suffering from encephalitis were as follows:

MONTHLY INCIDENCE:

It is evident from this study spread over 21 months, that the incidence of encephalitis was almost negligible in the later part of the rainy season and early part of the winter (Table 1). Maximum incidence was observed in the summer. The overall incidence was about 1·25 per cent of total admission in paediatric ward.

TABLE 1—SHOWING MONTHLY INCIDENCE OF 38 CASES STUDIED

Year	Months												Total
	Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sept.	Oct.	Nov.	Dec.	
1961	—	—	—	—	—	1	2	2	—	—	—	3	8
1962	4	4	3	6	1	3	5	1	—	—	—	—	27
1963	—	3	—	—	—	—	—	—	—	—	—	—	3

CLINICAL FEATURES:

Onset—In the majority of cases (92 per cent) the onset was fairly uniform and abrupt. No history of significant past illness was available and there was no evidence or account of any prodromal symptoms preceding the clinical onset, such as upper respiratory tract infection, gastro-

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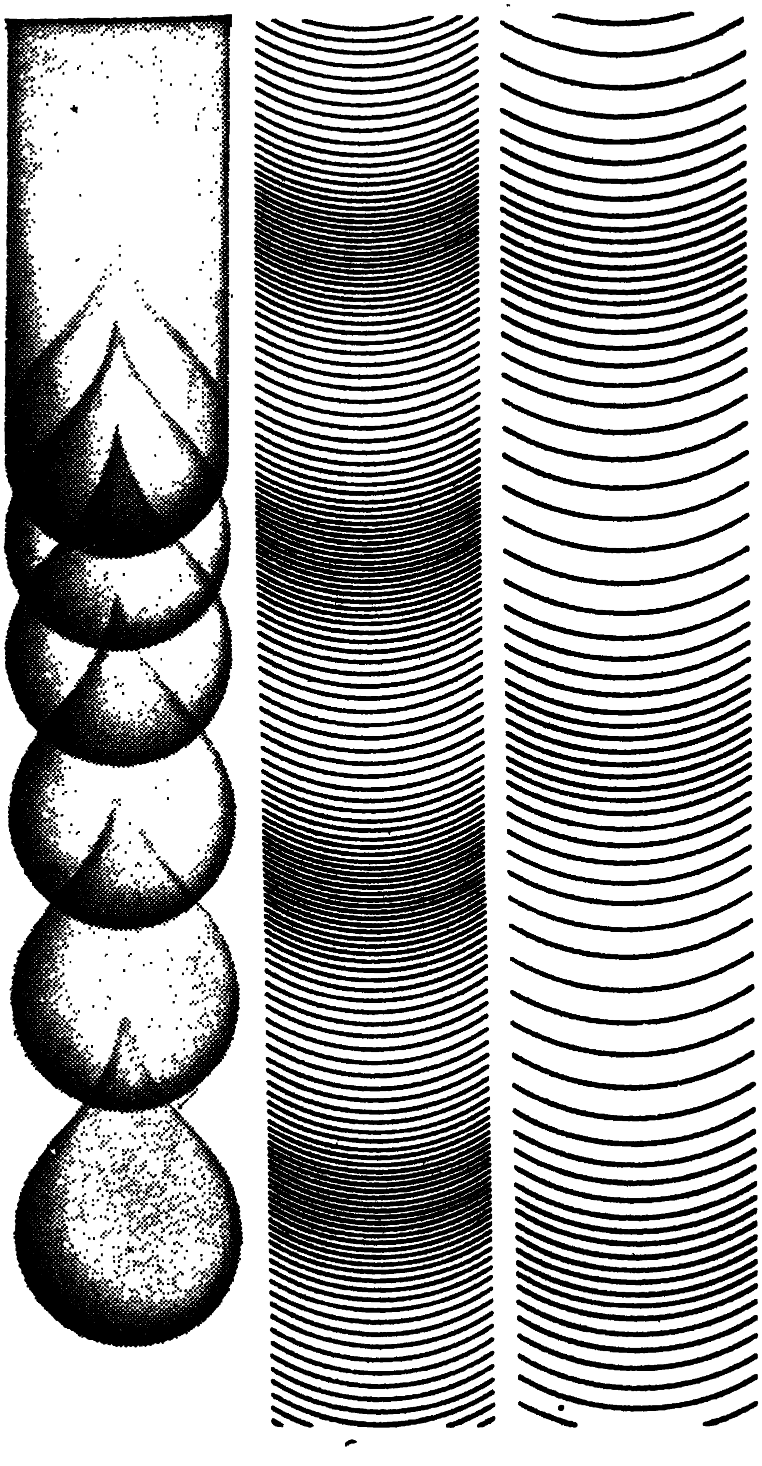

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intestinal upset, rash, etc. In the remaining 8 per cent of cases the onset was not so abrupt and stormy, and complete symptom complex of encephalitis took 24 to 72 hours to develop fully.

Age incidence—In the present series, only children were studied. This is at variance with the reported studies on encephalitis from different countries (Cleland and Campbell, 1919 ; Hammon, 1941 ; Khan, 1954) which included adult cases also. In the present study (Table 2), the incidence was found maximum in the first two years of life (65·8 per cent) and then the incidence gradually decreased with increase in age. No case was observed in children above 7 years of age.

TABLE 2—SHOWING INCIDENCE OF ENCEPHALITIS IN DIFFERENT AGE GROUPS

Age group	No. of cases	Per cent
Up to 1 year	15	39·5
Above 1 up to 2 years ...	10	26·3
,, 2 ,, 3 ,, ...	4	10 6
,, 3 ,, 4 ,, . .	3	7·9
,, 4 ,, 5 ,, ...	3	7·9
,, 5 ,, 6 ,, ...	2	5·2
,, 6 ,, 7 ,, ...	1	2·6
,, 7 years	—	—

TABLE 3—SHOWING DISTRIBUTION OF CASES ACCORDING TO SEX

Age group	Male		Female	
	No.	%	No.	%
From 0 to 1 year ...	10	26·3	5	13·2
Above 1 up to 2 years ...	8	21·0	3	5·2
,, 2 ,, 3 ,, ...	3	7·9	1	2·6
,, 3 ,, 4 ,, ..	2	5·2	1	2·6
,, 4 ,, 5 ,, ...	1	2·6	2	5·2
,, 5 ,, 6 ,, ...	1	2·6	1	2·6
,, 6 ,, 7 ,, ...	1	2·6	—	—
,, 7 years	—	—	—	—
Total	26	68·4	12	31·6

Sex incidence—From Table 3, the disease appears to show a male sex preponderance, 68·4 per cent being male and 31·6 per cent female. This is especially marked in the age group 0-3 years. This seems to be statistically insignificant because of the small number of cases studied, and secondly it could possibly be due to the comparatively large number of male admissions in the paediatric ward. Although authors from India and abroad have reported a sex predilection (Cleland and Campbell, 1919 ; Gour, 1954 ; Swami and Chari, 1955), others like Leake *et al.* (1934) reported equal incidence at St. Louis.

Initial manifestations—The initial presenting symptoms (Table 4) described by attendants of patients were soon followed in quick succession by other symptoms in some cases, while in still others symptoms like pyrexia, convulsions, involuntary movements, etc., appeared within 24 to 72 hours of hospitalisation.

TABLE 4—SHOWING COMMON INITIAL PRESENTING SYMPTOMS

Symptom	No. of cases	Per cent
Fever	22	57·9
Convulsion	20	52·6
Involuntary movement ...	12	31·6
Cough	11	28·9
Vomiting	10	26·3
Unconsciousness	10	26·3
Twitchings on face	10	26·3
Diarrhoea	8	21·0
Dyspnoea	8	21·0
Drowsiness	6	15·8
Irritability	6	15·8
Chill	6	15·8
Inability to support neck and trunk	4	10·5

Fever was present only in 57·9 per cent cases initially. About half of the children had convulsions. Variable degree of loss of consciousness was present in 42·1 per cent of children. 4 cases presented with inability to support neck and trunk. Besides, some interesting modes of onset were also seen.

CASE REPORT

A male child, aged 4 years, was admitted in the paediatric ward on 13-5-62 with sudden development of weakness of trunk and neck musculature while playing. On clinical examination the child was found to have a low grade fever (99·6°F) and flaccidity of neck and trunk muscles. There were no convulsions and loss of consciousness. Pulse rate was 96/min., regular, and blood pressure was 96/60 mm. of Hg. Pupils were normal. Peripheral blood examination and C.S.F. examination were normal. The patient was put on tetracyclines and corticosteroids and complete clinical recovery occurred in 11 days.

Common symptoms and signs—These have been summarised in Tables 5 and 6 respectively. Convulsions were present in 26 children (68·4 per cent), 6 children having developed it after hospi-

TABLE 5—SHOWING COMMON SYMPTOMS OBSERVED

Symptom	No. of cases	Per cent
Fever	33	86·8
Convulsion	26	68·4
Involuntary movement :	17	44·7
(a) All four limbs, 5 cases		
(b) Both upper limbs, 1 case		
(c) Right half of body, 7 cases		
(d) Left half of body, 3 cases		
(e) Alternate right half to left half, 1 case		
Unconsciousness :	12	31·6
Tremor and twitching ...	12	31·6
(a) Face muscles, 11 cases		
(b) Tongue, 1 case		
Conjugate ocular deviation ...	11	28·9
Cough	11	28·9
Diarrhoea	11	28·9
Vomiting	11	28·9
Chill	11	28·9
Lethargy and drowsiness ...	9	23·7
Irritability	8	21·0
Dyspnoea	7	18·4
Semiconsciousness	6	15·8
Froth from nostrils and mouth	5	13·1
Weakness of trunk and neck muscles	4	10·5
Paralysis of limbs	4	10·5
Constipation	2	5·2
Retention of urine	2	5·2
Rigidity of all four limbs ...	1	2·6
Headache and delirium ...	1	2·6

TABLE 6—SHOWING COMMON SIGNS ELICITED

Sign	No. of cases	Per cent
Tachycardia (proportional to age)	32	84·2
Convulsion	26	68·4
Absent abdominal reflexes ...	23	60·5
Extensor plantar reflex . .	22	57·9
Dilated pupils	21	55·2
Exaggerated deep jerks	18	47·3
Involuntary movements .	17	44·7
Twitchings of face muscles and tongue	12	31·6
Unconsciousness	12	31·6
Conjugate ocular deviation ...	11	28·9
Bronchitis	9	23·7
Drowsiness	9	23·7
Flexor plantar reflex	9	23·7
Irritability	8	21·0
Meningeal irritation (neck rigidity, and Kernig's sign+ve) ..	8	21·0
Dyspnoea	7	18·4
Semiconsciousness	6	15·8
Pulmonary oedema	5	13·2
Weakness of trunk and neck muscles	4	10·5
Absent corneal reflex	4	10·5
Sluggish deep jerks	4	10·5
Hypotonia of muscles	4	10·5
Absent deep jerks	4	10·5
Constricted pupils	3	7·9
Hemiplegia right side ...	3	7·9
Hemiplegia left side	1	2·6
Facial palsy (left side) ...	1	2·6

talisation. In 28·9 per cent of children diarrhoea and vomiting were additional features. Paralysis of limbs occurred in 10·5 per cent of cases. Uncommon features observed were retention of urine 2 cases, headache and delirium in 1 case. Twitchings of face muscles occurred in 11 cases (28·9 per cent) while that of the tongue in 1 case only.

Temperature—This was raised to a variable extent in 86·8 per cent of cases (33 children), while 13·1 per cent children had normal temperature throughout.

In 17 children (44·72 per cent) the temperature ranged between 98·4°F and 102°F and in 34·2 per cent remained between 102°F and 104°F. Mortality was cent per cent in children who had initial temperature above 104°F (Table 7) . This is statistically insignificant, as the number of cases is too small.

TABLE 7—SHOWING RANGE OF TEMPERATURE AND RELATIONSHIP TO MORTALITY

Temperature range	No. of cases	No. of deaths	Mortality per cent
Up to 98·4° (Normal) ...	5	—	—
Above 98·4° up to 100° ...	6	—	—
„ 100° „ 102° ...	11	2	18
„ 102° „ 104° ...	13	3	23
„ 104° „ 106° ...	2	2	100
„ 106° ...	1	1	100
Total ...	38	8	21

Duration of pyrexia—For this observation, fatal cases and those who left against medical advice before the temperature returned to normal were excluded. One case continued to have low grade pyrexia even when under hospitalisation for 44 days. Majority of patients became afebrile in 1 to 9 days. Only in 1 case pyrexia did not last for more than 1 day (Table 8).

Pulse—The pulse rate corresponded in majority of cases with increase in temperature, except in one case who had relative bradycardia.

TABLE 8—SHOWING DURATION OF PYREXIA (21 CASES)

No. of days	No. of cases	Per cent
Up to 1 day	1	4·76
Above 1 up to 3 days	4	19·04
„ 3 „ 6 „	7	33·32
„ 6 „ 9 „	4	19·04
„ 9 days	5	23·80

Pulmonary signs—8 children (29 per cent) at the time of admission showed signs of bronchitis along with features of encephalitis. 5 cases had pulmonary oedema either at the time of admission or terminally, and eventually all expired.

NEUROLOGICAL FINDINGS :

These are as shown in Tables 9-12.

Pupillary reaction—Variations in the size and reaction of pupils were observed in about 70 per cent of cases. Cases with fixed pupillary reaction signalled a grave prognosis, while those with sluggish reaction had a guarded prognosis. The findings are presented in Table 9.

TABLE 9—SHOWING CHANGES IN PUPILLARY REACTION (38 CASES)

Pupillary change	No. of cases	Per cent
No change (normal)	11	28·9
Dilated	21	55·3
(a) Sluggish reaction 12 cases		
(b) Fixed - 9 cases		
Constricted	3	7·9
(a) Sluggish reaction -2 cases		
(b) Fixed 1 case		
Unequal with variable reaction	3	7·9

Alteration in the state of consciousness—Gross alteration in the state of consciousness was present in 47·4 per cent of cases. 31·6 per cent (18 children) were in a comatose state, out of which 7 children subsequently expired. Undue irritability was present in 21 per cent of cases. There was no change in the state of consciousness in 3 cases, while 9 cases (23·7 per cent) were drowsy only. These changes have been summarised in Table 10.

Cranial nerves—Upper motor neurone type of unilateral facial palsy was seen in one only, which recovered completely during the patient's stay in the hospital. Other cranial nerves were not affected.

TABLE 10—SHOWING NEUROLOGICAL CONDITION (CHANGES IN THE STATE OF CONSCIOUSNESS) (38 CASES)

Symptom	No. of cases	Per cent
Deep coma	12	31·6
Semi-coma	6	15·8
Drowsiness	9	23·7
Undue irritability	8	21·0
No change	3	7·9

Motor system—Paresis and paralysis of various parts of the body were seen in 26·3 per cent of cases (Table 11). All the surviving cases improved completely over a period of time. None of the cases went in for residual neurological features or sequelae.

TABLE 11—SHOWING DISTRIBUTION OF PARESIS OR PARALYSIS (10 CASES)

Lesion	No. of cases	Per cent
Flaccid paralysis of muscles of neck and trunk	4	10·5
Right-sided hemiplegia	3 (2)	7·9
Left-sided hemiplegia	1 (1)	2·6
Facial palsy (U.M.N.)	1	2·6
Rigidity of all the limbs	1	2·6

N.B.—Figures in parentheses denote number of cases expired. U.M.N. stands for upper motor neurone type.

Organic reflexes—Deranged functions of these reflexes were seen in a very small number of cases and were in the form of retention of urine in 2 cases who had normal bladder control previously. None of these cases had any evidence of cord lesion.

Superficial reflexes—About 60·5 per cent of cases showed absence of superficial abdominal reflexes. In children the plantar reflex is usually taken with some scepticism. The final outcome and its relationship to plantar response is shown in Table 12. In 18 cases who presented with coma or semicoma, 7 cases expired out of 12 cases who had bilateral extensor plantar response.

INVESTIGATIONS :

Leucocyte count—The total leucocyte count of 37 cases is summarised in Table 13. The lowest count obtained was 4,900/c.mm. and the highest 19,400/c.mm.

TABLE 12—SHOWING RESPONSE TO PLANTAR REFLEX AND RELATIONSHIP TO MORTALITY IN 38 CASES

Age group	Plantar response				
	Bilateral extensor	Bilateral flexor	Absent	Equivocal	Variable on two sides
Less than 2 years :					
(a) With coma	8 (2)	—	5 (2)	1	—
(b) Without coma	6 (1)	5	—	—	—
More than 2 years :					
(a) With coma	4 (3)	—	—	—	—
(b) Without coma	4	4	—	—	1
Total	22 (6)	9	5 (2)	1	1

N.B.—Figures in parentheses denote the number of fatal cases in each group.

TABLE 13—SHOWING TOTAL LEUCOCYTE COUNT

Total leucocyte count in different ranges (per c.mm.)	No. of cases
4,500— 6,000	2
6,100— 9,000	5
9,100—12,000	18
12,100—15,000	7
15,100—20,000	5

Differential leucocyte count—Polymorphs 72-82 per cent was observed in about 87 per cent of children.

Cerebrospinal fluid—The cerebrospinal fluid (C.S.F.) obtained by lumbar puncture was invariably under tension and uniformly clear. The results of analysis are given in Tables 14 to 16.

TABLE 14—SHOWING CHANGES IN C.S.F. PROTEINS

C.S.F. proteins (mg./100 ml.)	No. of cases
20— 40	26
41— 60	11
61—100	1

TABLE 15—SHOWING CHLORIDE LEVELS IN C.S.F.

Chloride level (mg./100 ml.)	No. of cases
600—670	6
680—750	30
760—800	2

TABLE 16—SHOWING CELL COUNT IN C.S.F. (38 CASES)

No. of cells/c.mm. of C.S.F.	No. of cases
Up to 5 cells	29
6—10 cells	3
11—20 cells	3
Above 20 cells	3

Sugar levels were not estimated quantitatively but sugar was present in all the cases on qualitative estimation.

DISCUSSION

Clinical and laboratory data obtained in various outbreaks of acute infections of the central nervous system during the past half a century indicated that such epidemics were due to acute encephalitis, first classical description having appeared in 1917.

The first major epidemic in India broke out in 1954 at Jamshedpur and similar outbreaks in successive months were reported from Northern India (Khan, *loc cit.* ; Taneja, 1955 ; Gour, 1956 ; Seal and Ghose Chowdhury, 1956). Encephalitis has been accepted as a clinical syndrome, although its aetiological agent still remains unknown. Of the various suspected aetiological agents, such as bacterial, viral and toxic substances, the viruses are now being incriminated as being responsible for many of the severe epidemics of the world. It is customary to designate the disease by the name of its place of occurrence. In many outbreaks in this country and abroad, viruses have been presumed to be the causative agents because of our failure to find out any other convincing aetiologic agents.

In the present study, we had 38 cases diagnosed on clinical grounds. In these cases no other diagnostic label was possible on follow-up and investigations like cerebrospinal fluid examination. The clinical picture was remarkably uniform. 92 per cent of children were taken ill abruptly with pyrexia, variable degree of loss of consciousness, convulsions, neurological findings and with a high mortality rate. Investigations in the majority of cases showed more or less normal C.S.F. and a predominantly polymorphonuclear leucocytosis in peripheral blood.

Mild cases of encephalitis do occur which would otherwise have been missed, but for the positive virological and serological investigations, as exemplified by a percentage of cases of St. Louis encephalitis (Muckenfuss *et al.*, 1934 ; Hempelmann, 1934). But in the present series only those cases were included which showed some evidence of encephalon involvement. These cases occurred sporadically throughout the year except in winter months, but a majority of cases occurred during summer and early rainy season. This strongly suggests an infective nature. The occurrence of fulminant and less fulminant cases, and its predilection for infants and children, leucocytosis and pyrexia in the majority of cases, are strong points towards such an aetiology.

No bacterial, protozoal or metazoal agent could be labelled definitively as to its aetiology, and the consensus of opinion today favours the causative agent to be a virus. Supportive evidences which point to a virus are, selection of relatively healthy children, presence of leucocytosis with a more or less normal cerebrospinal fluid, and failure of response to chemotherapy significantly. The exact nature of the virus, however cannot be stated because of lack of facilities for virological studies in the hospital.

In the present series, 92 per cent of cases belonged to the age group 0-5 years, while 65·8 per cent children were under 2 years of age. Incidence decreased with increase in age, so much so that in the present series none of the cases affected belonged to above 7 years age group. In their study of 301 cases, Bajpai *et al.* (1960) observed 66·7 per cent of children belonged to the age group 0-5 years. While at Agra and Nagpur the percentage of children of this age group affected was 67·7 and 69·6 per cent respectively. This is in contrast to the Jamshedpur epidemic where the incidence in comparable age groups is much lower (Berry *et al.*, 1959 ; Mathur and Prasad, 1959 ; Seal and Ghose Chowdhary, 1956).

This disease appeared to show a male sex preponderance, affecting 68·4 per cent male and 31·6 per cent female patients. This compares well to 61·3 per cent male and 39·7 per cent female reported by Bajpai *et al.* (1960). The sex incidence was found to be equal in St. Louis epidemic (Leake *et al.*, *loc. cit.*).

The polymorphs in peripheral blood, and normal cerebrospinal fluid findings in the majority of cases confirm previous reports of other Indian authors.

Duration of pyrexia in majority of cases was 1-9 days, with only one exception in which case a low grade pyrexia continued for more than 44 days. The 3 cases who had initial temperature above 104°F proved fatal, but this observation is statistically insignificant because of the small number of cases. 5 cases were apyrexial throughout their stay in hospital. The overall mortality was 21 per cent, being cent per cent in cases who had initial temperature above 104°F.

26·3 per cent (10 children) had neurological features of paresis or paralysis, either flaccid or spastic. 3 cases (7·9 per cent) expired out of 4 cases who had developed hemiplegia. 1 case presented with extra-pyramidal type of rigidity of all the limbs but improved completely later without leaving any residual neurological sequelae. No sensory changes were observed in any of the cases.

All the patients were given parentral tetracyclines and corticosteroids in therapeutic doses, but no significant effect either on the final outcome as regards complications and mortality was established. The consensus of opinion remains that they are not much useful excepting in cases having secondary bacterial infection and shock.

SUMMARY

38 cases of encephalitis admitted in Hamidia Hospital at Bhopal are reported for their special features.

Aetiology, clinical features with special reference to neurological features and investigations are discussed.

Role of corticosteroids and tetracyclines in the management is discussed.

ACKNOWLEDGMENT

The authors are grateful to Dr. Narendra Singh, Dean, Gandhi Medical College, Bhopal, for permission to report this study, and to Dr. S. M. Misra, Professor and Head of the Department of Medicine, Gandhi Medical College, Bhopal, for valuable guidance and encouragement in this study.

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PHOSPHATASE REACTION OF STAPHYLOCOCCI ISOLATED FROM OCULAR LESIONS

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The recognition of pathogenicity of staphylococci depends upon a combination of various characters (Burns and Holtman, 1960), though some of the biological properties are of particular importance such as production of coagulase (Mirolli, 1931), α-haemolysin (Marks, 1952), desoxyribonuclease (Jeffries, 1961), hyaluronidase (Vogelsang *et al.*, 1962) and phosphatase (Barber and Kuper, 1951) as they are almost always associated with the virulence of these organisms. However, at present there is universal agreement that the coagulase positive staphylococci should be taken for granted as pathogenic and the value of any other test as a criterion for the pathogenicity would depend on its correlation with the coagulase production.

Many workers have interested themselves in the reactions that might parallel the coagulase reaction. Barber and Kuper (*loc. cit.*) found cent per cent correlation between phosphatase and coagulase tests. Since then due to the simplicity of the reaction a number of workers have evaluated this reaction with conflicting results to the original observation.

The present communication covers the observations on phosphatase reaction of staphylococci isolated from ocular lesions.

MATERIAL AND METHOD

1. *Strains*—The staphylococcal strains were isolated from patients with eye diseases like blepharitis, stye, corneal ulcer, conjunctivitis, cataract, etc. The patients either attended the outpatients department or were admitted to the inpatients section of Gandhi Eye Hospital, Aligarh. The strains were isolated on blood agar plates and stocked in agar stab cultures in refrigerator (4°C) until used for the study.
2. *Coagulase test*—Both slide and tube tests were performed (Cruickshank, 1960).
3. *Phosphatase reaction*—Phenolphthalein-diphosphate (pentasodium[†]) was added to the melted nutrient agar in the concentration of 0·01 per cent and the plates were poured. The strains were inoculated lightly on the plates so as to give discrete colonies after 20 to 22 hours of incubation at 37°C. The plates were then exposed to ammonia vapours for a few seconds. If the colonies of staphylococci turned pink the test was positive (Barber and Kuper, *loc. cit.*).

RESULTS

A total of 317 staphylococcal strains was tested for the phosphatase reaction, out of which 209 strains were coagulase positive and 108 were coagulase negative.

All the coagulase positive strains were phosphatase positive. On the other hand only in 33 coagulase negative strains phosphatase reaction was negative (Table 1).

TABLE 1 SHOWING PHOSPHATASE REACTION OF STAPHYLOCOCCI

	Phosphatase positive	Phosphatase negative
Coagulase positive ...	209 (100%)	0
Coagulase negative	75 (69·4%)	33 (30·6%)

DISCUSSION

In the present series phosphatase production was observed among all the coagulase positive strains. Nevertheless 69·4 per cent of coagulase negative strains were also positive for the test.

Barber and Kuper (*loc. cit.*) reported that all the coagulase positive strains were phosphatase positive and all the coagulase negative strains were phosphatase negative. This study concurred with the former finding but it was also observed that many of the coagulase negative strains produced this enzyme. Similar results have been recorded by a number of workers (Gupta and Chakravarti, 1954 ; Rangam and Katdare, 1954 ; Pal and Ray, 1962 ; Willis and Turner, 1962) who found that 10 to 25 per cent of coagulase negative strains were phosphatase positive. However, in this group a considerably higher percentage (69·4 per cent) of coagulase negative organisms were found to be positive for this reaction. The variation could be due to the differences in the substrate employed by various workers or that these strains might have been antibiotic resistant due to frequent and routine instillation of antibiotics in the eyes in the wards. In case of coagulase positive staphylococci Gillessen and Ruda (1958) observed that the amount of phosphatase produced by antibiotic resistant strains of ***Staph. aureus*** was much higher than the amount produced by antibiotic sensitive strains.

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The quantitative studies on phosphatase production of staphylococci in literature have revealed that on an average coagulase positive strains produce more phosphatse than negative strains but a few of the coagulase positive strains at the same time produce less phosphatase than negative ones (Pan and Blumenthal, 1961 ; Cannon and Hawn, 1963). Considering these quantitative studies it also becomes apparent that it is not possible to demarcate between coagulase positive and negative strains on the basis of phosphatase reaction.

It may be concluded that phosphatase reaction serves no useful purpose as a criterion for the pathogenicity of staphylococci, particularly if it is positive. Further, the test loses its importance when other tests are available which give much better correlation with the coagulase test, such as α-haemolysin (Marks, *loc. cit.*) desoxyribonuclease (Jeffries, *loc. cit.*), hyaluronidase (Vogelsang *et al.*, *loc. cit.* ; Bal *et al.*, 1964) and pigment production on glycerol mono-acetate medium (Willis and Turner, *loc. cit.*). However, if the phosphatase test is negative it may be presumed that coagulase test will also be negative.

SUMMARY

Three hundred and seventeen strains of staphylococci were tested for phosphatase reaction.

All the coagulase positive strains were phosphatase positive, but at the same time 69·4 per cent of coagulase negative strains were also positive for the test.

Phosphatase reaction cannot be used as a basis for differentiation of coagulase positive and negative staphylococci.

ACKNOWLEDGMENT

The technical assistance of Mr. Chandra Mohan is thankfully acknowledged.

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PRACTITIONERS' SERIES

SHOCK

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The term shock has as yet no universally accepted definition. It may be defined as an extremely complex phenomenon, clinically composed of an impressive symptom complex which is the chief outcome of a disordered haemodynamics characterised by an acute fall of arterial blood pressure due to a disproportion between vascular capacity and circulating blood volume. Morphological change and functional impairment occurs if peripheral circulation decreases to an extent, where a normal biological process cannot take place, leading to inadequate tissue perfusion, tissue hypoxia, hypoxic metabolism, metabolic acidosis and finally irreversible tissue damage depending on the degree and duration of oxygen deficiency.

PATHOGENESIS

The chief pathologic finding in various types of shock is the acute arterial hypotension. For the maintenance of normal arterial B.P. four mechanisms are responsible: optimum cardiac output, venous return to the heart, optimum blood volume and peripheral resistance of blood vessels. Any interference to the above mechanisms initiates the onset of shock. An aetiopathologic classification of shock is mentioned below : (A) Decreased cardiac output : (1) Myocardial infarction. (2) Myocarditis (diphtheria). (3) Massive pulmonary embolism. (4) Ventricular compression (cardiac tamponade from tension of pericardial fluid thereby limiting ventricular distensionability). (B) Decreased blood volume : (1) Acute haemorrhage from any source. (2) Plasma loss from severe burn and crushed injury. (3) Dehydration and salt depletion in : (a) Vomiting and diarrhoea e.g., pyloric stenosis, intestinal obstruction, (b) polyuria and ketosis e.g., diabetes mellitus, (c) excessive sweating e.g., heat exhaustion, (d) Addison's disease. (C) Altered and decreased peripheral resistance to blood flow (by pooling mechanisms): (1) Reflex mechanisms e.g., syncope, following trauma to solar plexus or to testicles, following perforation of a hollow viscus, acute pancreatitis, and following pain (from any severe type). (2) Capillary damage from toxins e.g., diphtheria, pneumonia. (3) Sudden suprarenal failure from meningococcal septicaemia. (4) Drugs e.g., ganglion blocking agents e.g., hexamethonium and spinal anaesthesia. (5) Anaphylactic shock (exact mechanisms unknown but lack of vascular tone is believed). (D) Diminished venous return: (1) All the clinical conditions of groups (B) and (C). (2) Pericardial effusion (inadequate venous filling in heart). (3) Toxic states—overwhelming infection in gram-negative toxin-liberating bacteria where endotoxin (lipopolysaccharide) has a sympathetic blocking action causing intense spasm specially of blood vessels of visceral organs, thereby large amount of circulating blood is trapped in splanchnic venous bed causing diminished venous return.

No clear cut factors as enumerated above play a role for the initiation of shock. Frequently a combination of several factors play at the onset. Thus a shock in a major surgical operation is due to: loss of blood, plasma, dehydration from excessive handling of tissues, infections and anaesthesia. Similarly, the very pain of myocardial infarction or acute massive pulmonary embolism may precipitate shock.

CLINICOPATHOLOGIC CLASSIFICATION

Here shock is classified and grouped according to the dominant disorder of haemodynamics observed in varieties of clinical states, and type of clinical status presented.

Surgical shock—It results from acute diminution of circulating blood volume from loss of blood or plasma. (a) Haemorrhage—acute, from any source. (b) Loss of plasma e.g., burn, crushed wounds. (c) Operative or postoperative shock is due to a combination of loss of blood, plasma, infections and anaesthetics.

Medical shock—There is no loss of blood or plasma but loss of fluid and electrolytes resulting in diminution of blood volume: (a) Diarrhoea and vomiting—any form of gastro-enteritis, colitis, pyloric stenosis, intestinal obstruction. Vomiting causes loss of chloride ions but diarrhoea causes loss of sodium ions. (b) Diabetes—It is associated with both loss of fluid and electrolyte by way of polyuria and ketosis. (c) Addison's disease—Here excessive sodium ion is lost by the kidney due to lack of control of electrolytes by adrenal cortex. Vomiting and diarrhoea add to dehydration. (d) Any form of severe infection. (e) Myocardial infarction. (f) Acute pericarditis.

Neurogenic shock—There is no loss of blood, plasma, fluids, electrolytes, but from reflex vasodilatation with consequent pooling blood into the splanchnic area—thus decreasing the amount of blood taking an effective part to maintain B.P. resulting in deficient venous return, cardiac output and fall of blood pressure. They are: (a) Perforation of peptic ulcer. (b) Blow to solar plexus or to testicle. (c) Acute pancreatitis. (d) Severe pain from other causes.

Miscellaneous types—Here the exact mechanism is unknown but a general vasodilatation due to lack of vascular tone is believed to be the cause. They are: (a) Anaphylactic shock. (b) Histamine shock.

EVALUATION OF SHOCK

Diagnosis of shock in early stage depends on the knowledge of the clinical conditions where it can develop and a clear idea of the clinical features of shock.

The clinical features of shock are very impressive and can be suspected with the very appearance of one or more of the following characteristic features: Extreme weakness, shivering, apathy or sometimes restlessness, consciousness is generally retained without confusion, pallor and cold skin, rapid, low-volume arterial pulse, subnormal temperature, acute fall of arterial pressure, venous pressure is usually low, and oliguria or anuria.

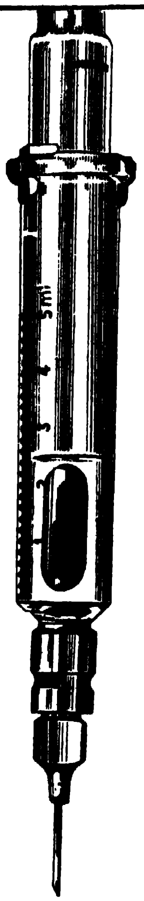
With the knowledge of the above clinical picture, the patient's status can be evaluated further by the following additional measures:

(a) Periodic measurements of blood pressure, pulse pressure and respiration. (b) Measurement of central venous pressure. (c) Measurement of hourly urine volume by means of an indwelling Foley's catheter. (d) Where facility exists, accurate measurement of circulating blood volume. (e) Determination of blood pH and electrolytes e.g., K, Cl and estimation of blood sugar and coagulation studies. (f) E.C.G. studies both for diagnostis, prognostic and therapeutic value.

MANAGEMENT OF SHOCK

In the management of shock it is considered that therapy must be instituted before final phase is reached, and every effort must be directed to restore the systolic blood pressure to a value of 90 mm. of Hg as soon as possible.

Restoration of blood pressure—The various methods by which the objective can be achieved are mentioned below but the method to be followed depends on the primary cause of shock.



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Rest in bed—Absolute rest is essential. The patient should lie in supine position except in certain types of head or chest injuries where head and chest may have to be raised. If the shock is profound and rapidly progressing the foot end of the bed should be raised 12 to 18 inches above the head end. If the patient vomits as in deep shock the head should be kept low and turned to one side.

The air passages are cleaned to maintain a good airway and kept free to prevent aspiration. A suction apparatus is to be kept ready at bedside where available. The patient should not be moved or his injuries are not to be manipulated till shock has been overcome by other means.

Warmth—Patient is to be kept warm by suitable coverings. External heat is to be applied very carefully specially to the extremities.

Oxygen—It may be used on a known principle that when oxygen is efficiently applied (6 to 8 litres/minutes) in a shocked patient there is a rise in systolic blood pressure of 20 mm. of Hg or more, if oxygen is prematurely discontinued the blood pressure falls often rapidly. The response is marked when there is respiratory depression. One patient may require a considerable volume of oxygen and it is harmful to economise it.

Sedation—Adequate sedation is essential—the dose being dependent on symptoms. Sedatives are very useful in restless and apprehensive cases. In most cases initial 15 mg. of morphine is sufficient. In severe shock, it is wise to give very slow intravenous morphine but diluted. It should not be given to stuporose or comatose patients. Morphine is absolutely contra-indicated in Addison's disease or acute suprarenal failure.

Fluids—Blood transfusion—Whole blood is the fluid of choice in haemorrhagic shock. It is valuable in other types of shock specially when doubt exists as to the cause of shock. The volume of blood to be infused depends on the amount of blood lost and degree of shock prevailing, guided by blood pressure and pulse pressure. The amount may be given in short time under pressure. The transfusion have to be continued till source of haemorrhage is controlled. Intravenous transfusion is dangerous in presence of either increased venous pressure or pulmonary oedema. If it is indicated even in these states it is wise to consider to give it by intra-arterial route.

Intra-arterial blood transfusion—It is indicated in progressive haemorrhagic shock which is not controlled by I. V. blood transfusion. It has initial beneficial effect. When the aortic semilunar valves close (if they are open, retrograde blood under pressure closes them)—the blood under pressure is forced into coronary, as well as to the periphery, no strain is put to the myocardium, but the myocardium receives the benefit of oxygenated blood. Even after the transfusion is over, the heart beats efficiently and effectively. If further transfusion is necessary, blood plasma or plasma substitute can be used I.V. at a moderate rate.

In emergency Group 'O' Rh negative blood can only be used after cross matching. Nonoxygen carrying fluid if used by intra-arterial route causes gangrene. Blood suitably matched is given into the artery in a retrograde manner under pressure. Artery of choice is radial—in severe cases brachial artery may be used. Positive pressure is achieved by connecting the air vent of blood bottle with tubing connected to the bellows of sphygmomanometer or suitably by Binghams arterial transfusion apparatus. Blood is kept on flowing by raising the pressure in the blood bottle in between 160-200 mm. Hg by means of bellows. Great vigilance is essential so that delivery tube is clamped securely in a haemostat before the bottle becomes empty.

Plasma infusion—It is very valuable in an emergency where blood is being requisitioned and made ready for use. It is suitably used in cases of burn or in crushed injury where there is loss of plasma. Plasma is available in a dried state, has to be reconstituted with pyrogen-free injectable distilled water before it is used. It carries the risk of transmitting homologous serum jaundice.

Plasma substitutes—Dextran, a complex polysaccharide in 6 per cent solution, is commonly used. It is safer than Group 'O' blood when time factor prevents correct cross matching. According to the need and response of the patient one or two bottles of 500 ml. can be used, third bottle with caution but under no circumstances it should be exceeded as the blood undergoes dilution and its oxygen carrying capacity diminishes. If more fluid is required to combat shock, only correctly matched whole blood should be used. Dextran causes an enhanced rouleau formation and adds difficulty in cross matching of blood. Hence a sample of blood should be drawn beforehand, a dextran infusion is started.

Fluids and electrolyte solutions—This therapy is indicated in the following conditions of shock: (a) In dehydration with consequent loss of electrolytes. (b) As an initial treatment where blood transfusion is awaited. (c) After initial shock is combated by other means—for the maintenance of fluid and electrolyte volume and blood pressure. Common form of solutions used are: normal saline solution, normal saline with 5 per cent glucose, 5 per cent glucose solution and 1/6 molar lactate solution.

Provided there is no venous engorgement and pulmonary oedema, the initial flow of fluids is allowed in sufficient quantity to restore the circulatory state. Quantity of total fluid requirement is guided by: (a) amount of dehydration present, (b) basal water requirement during 24 hours time and (c) abnormal water loss during 24 hours time. The sum of (a), (b), (c) gives the amount necessary for ideal rehydration. In practice 2/3 of the calculated volume is given to prevent circulatory overloading. The choice of route is always intravenous in a state of shock.

Electrolytes—Amongst electrolytes, chiefly sodium requires recoupment from external source. Amount of sodium required to be recouped is determined by the following calculations—(lowest limit of normal Na level—observed Na level) body weight 0·62 in male and 0·52 in female is equal to Na deficit in mEq. P. That amount of Na to be corrected is given along with water to be recouped.

Drugs—The following groups of drugs are recommended for restoring arterial blood pressure: Sympathomimetics, analeptics, and corticosteroids.

(1) Sympathomimetic drugs: These drugs raise the blood pressure by producing peripheral vasoconstriction. Methedrine and noradrenaline are more satisfactory as they exert little or no effect on pulse rate and they act humorally.

Methedrine: It is given 30 mg. I.M. or I.V. stat, and repeated after 15 minutes. Overdosages cause cerebral excitation and convulsion. It is very valuable in shock due to hypotension after use of spinal anaesthesia or ganglion-blocking drugs.

Noradrenaline: This is the most effective drug for controlling hypotensive shock in myocardial infarction. Suitable preparation is levophed (1-adrenaline bitartrate) 4 mg. is added to one litre of intravenous solution of blood, plasma, saline or glucose; so that 4 μg./ml. concentration is reached. This is given exclusively intravenously, speed of infusion is regulated by the degree of response to B.P. rise and maintained till a satisfactory level is achieved. This may be used till acute hypotensive emergency exists. It is very useful in those hypotensive states (not due to blood or fluid loss) which failed to respond satisfactorily after I.V. infusion alone.

(2) Analeptics: These have no action directly on the heart and blood vessels but they improve the circulatory state by improving respiratory rate. They are valuable when shock is associated with respiratory depression. Inj. nikethamide 2 ml. I.M. or I.V. repeated as necessary. Alternatively Inj. micoren 225 mg. in 1·5 ml. ampoules I.M. and can be repeated as necessary. It can be given I.V. diluted, very slowly—1 ampoule at least taking 10 minutes.

(3) Corticosteroids: Although it is not possible to demonstrate adrenal insufficiency in other types of shock except in Addison's disease or adrenal failure after suprarenal haemorrhage, corticosteroids have proved to be outstandingly effective in many cases. Dexamethasone-21-phosphate, 4 mg. injection I.V. or I.M. every 6 hourly. Alternatively, hydrocortisone haemisuccinate sodium 100 mg. I.V. is given every 6 hourly, with recovery the dose is tapered off. It is very useful in severe surgical shock, traumatic shock, burns or shock due to overwhelming infection and in anaphylactic shock.

Adjuvant measures—These measures are adjuvant to the above procedures to improve shock status of patient and to counteract hypotensive state.

Oral feed: In shock specially in surgical shock, patient is often thirsty. Here tolerated sips of water or normal saline can be given.

Antibiotics: Antibiotics of appropriate value are to be used in case of burns, injury, septicaemia and toxaemia following bacterial infections. The antibiotic commonly used are combinations of penicillin and streptomycin, tetracyclines, chloramphenicol or erythromycin.

Restoration of acid-base equilibrium: The degree of acidosis can be judged biochemically by the estimation of plasma bicarbonate where it is reduced in acidosis, e.g., diabetic ketosis, progressive shock of long duration. Total bicarbonate deficit is estimated by (lower limit of normal—observed level) × body weight × 0·62 in male and 0·52 in female = bicarbonate deficit in mEq./l. Suitable solution is 1/6th molar lactate used intravenously 4·2 ml. of 1/6th molar per kg. of body weight raises bicarbonate by 1 mEq./l. Hence total amount of molar lactate required to correct the deficit can easily be found out.

Hypothermia: Hypothermia is useful as a prophylactic measure but it is of little value where shock has already started and progressed.

Bandaging of extremities: In early stages of hypovolumic shock it may be of value and can be recommended. Such bandage is removed when satisfactory pulse volume is achieved. It is used in conjunction with other conventional method of combating shock.

Subsidiary measures—In the management of shock the following supportive measures are found to be effective in controlling shock, provided measures are taken in appropriate time.

. General prophylaxis: Promt diagnosis is essential for preventing onset. Gentle handling of injured part, prompt haemostasis, minimum handling of tissues at operation, limitation of exposure in burns, early correction of dehydration and electrolyte deficit, prevention of infection and judicious use of anaesthetics at operation, are all essential for prophylaxis.

First aid: Sometime the value of first aid in shock is questioned. It may be applied in the early stage of hypovolumic shock. Elevation of limb is the method of choice in first aid application of shock. Standing astride the head of the patient lying in supine, the legs are elevated. Such elevation helps the gravity drainage of blood from lower extrimity to the trunk. In some cases the effect can be enhanced by elevating the arms similarly.

Surgical intervention: The mode and time of surgical intervention depends on the clinical entity of the cases. In cardiac tamponade from pericardial effusion, an early aspiration of fluid either by thoracic or pericardial route helps to prevent or facilitate early recovery from shock. Similarly, prompt haemostasis in acute haemorrhage, early surgical operation in perforation of a viscus or in acute pancreatitis with biliary tract infection are called for. Late surgery is often beneficial in cases of severe burns where an initial shock has supervened.

Maintenance of charts: A chart indicating ½ hourly pulse, B.P., respiration rate, 1 hourly urine volume from an indwelling catheter, total intake and output of fluids are only of prognostic value in cases of shock.

Sympathetic blocking drugs: It is considered as one of the new approaches in therapy, in addition to existing methods. It is still in the experimental stage, possibility of applying in the later stages of shock to counteract the deleterious effect of increasing vasoconstriction is now being explored. The drug 'phenoxybenzamine' has a vasodilatory effect and counteracts the sympathetic vasoconstriction. It may be of value provided primary haemodynamic disorder is corrected. It has produced a promising result in endotoxic shock in experimental animal where an initial intense vasospasm is present.

SUMMARY

Various methods of combating an acute shock has been described. It is emphasised that each has to be judged according to its own merit on the basis of predisposing and immediate cause of shock.

It may be mentioned that even though a varieties of modern methods for combating shock is available; still shock is a problem specially in its aetiology and pathogenesis. It is utmost necessary to find out all the intricate factors and mechanisms that play in the exact aetiology and pathogenesis of shock.

SPECIAL ARTICLES

EMERGENCY GLOMECTOMY FOR STATUS ASTHMATICUS

A Preliminary Report

P. MADHOK, M.B., D.C.H., F.R.C.S.
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Status asthmaticus is a common medical emergency. These suffocating patients, with marked expiratory obstruction, can tax the ingenuity of any physician, when routine medications, such as adrenaline and aminophylline have been unsuccessful. That such a state of affairs can bring about a fatal outcome has been clearly shown by the series collected by Cardell and Pearson (1959).

In this series of 68 necropsies on patients dying of causes directly related to asthma, 55 (approximately 80 per cent) had died of status asthmaticus. This point is further emphasised by recalling the pathogenesis of the condition (Fig. 1).

The main feature of status asthmaticus is obstruction at the bronchiolar level caused by spasm, thickened mucosa and secretions. The vicious trio impedes the basic purpose of respiration, namely exchange of gases. As the attack

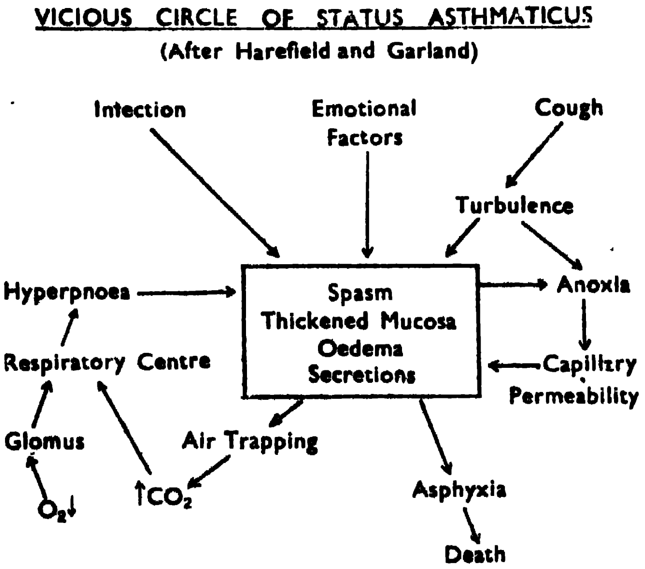

FIG. 1—SHOWING DIAGRAMMATIC REPRESENTATION OF THE PATHOGENESIS OF STATUS ASTHMATICUS

prolongs, the factor of increased capillary permeability comes into play—adding to the obstruction. If the attack continues unabated, patients die of asphyxia.

Introduction of corticosteroids in the treatment of asthma has, no doubt, changed the outlook on status asthmaticus. Five of our cases, however, failed to respond to prednisolone, despite the drug in high doses. There is a possibility that their number will increase, particularly from those asthmatics who are on long-term therapy, either self-designed or on the advice of the family doctor. There is also the hazard of side effects, the most important from the asthmatics' point of view being the diminishing capacity to fight infection due to suprarenal insufficiency.

After Nakayama (1961) and Overholt (1961) reported their somewhat identical results on carotid body removal for asthma from two different centres, we embarked on a series of glomectomy of our own and reported on our initial experiences of 50 cases (Madhok *et al.*, 1964). Seven of these were operated upon during status asthmaticus with instantaneous and complete relief. This encouraged us to include 18 more, making a total of 25. One of them has been excluded from this report due to lack of sufficient data. This is a report of 24 asthmatics operated upon as an emergency procedure during status asthmaticus. As far as is known, this is the first report on glomectomy for status asthmaticus.

MATERIAL AND METHOD

History and complete physical examination were the mainstay of the diagnosis. Blood counts, x-ray chest, and E.C.G. were used to exclude eosinophilia, lung pathology, and cardiac asthma respectively. Pulmonary cripples with gross emphysema and asthmatics with severe nasal allergy were excluded from this study.

As all patients in status had adrenaline and aminophylline administered prior to admission, and one or both of these drugs are repeated whilst in the wards, a minimum of 6 hours interval was allowed to lapse, prior to surgery being undertaken, in order to allow sufficient time for the drugs to act. Those patients who had received steroids were allowed 12 hours.

Five patients were failures of steroids. There were 12 males and 12 females. The youngest in the series was 17 and the oldest 50 years old.

Technique : The procedure carried out was fairly standard. 50 mg. of pethidine and 25 mg. of chlorpromazine were used to premedicate them. One hour later, surgery was carried out under local anaesthesia, using 1 per cent xylocaine (after skin testing).

A transverse incision, in the skin crease, at the level of the upper border of the thyroid cartilage was taken, the carotid bifurcation exposed and the carotid artery lifted using a rubber catheter. To provide greater mobility and leverage the superior thyroid artery was ligated and divided (if necessary). The adventitia of the carotid artery was stripped all round, over a distance of 1″ using the bifurcation as the centre point as recommended by Overholt (*loc. cit.*). The carotid glomus was removed. As for the difficulties of the operation we wish to draw attention to mainly two points:

First, that the carotid body like most anatomical structures is subject to variations. Initial difficulty in identifying the glomus prompted us to carry out 100 dissections on cadaveric carotids. As this is the subject of a separate communication, the results of these dissections will only be briefly stated.

The classical position of the carotid body has been described by Nakayama (*loc. cit.*) to be lying posteriorly at the bifurcation of the carotid artery. The size approximates that of a rice grain (Fig. 2).

This we found to be true in 82 per cent of our dissections. In the remaining 18 per cent, distribution was as follows:

13 per cent anteriorly, at bifurcation. 2 per cent duplicate anteriorly. 2 per cent duplicate, posteriorly. 1 per cent posteriorly on the external carotid, at the "take off" of the superior thyroid artery.

The size varied from 1 to 5 mm. Infants and children were found to possess a larger glomus—relative to their body size. The variations were

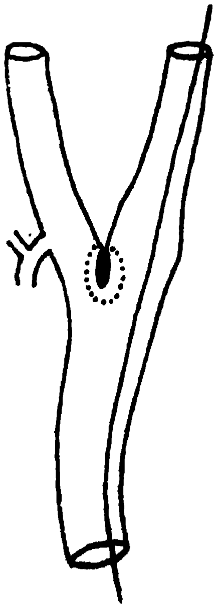

FIG. 2—SHOWING THE CLASSICAL POSITION OF THE CAROTID BODY

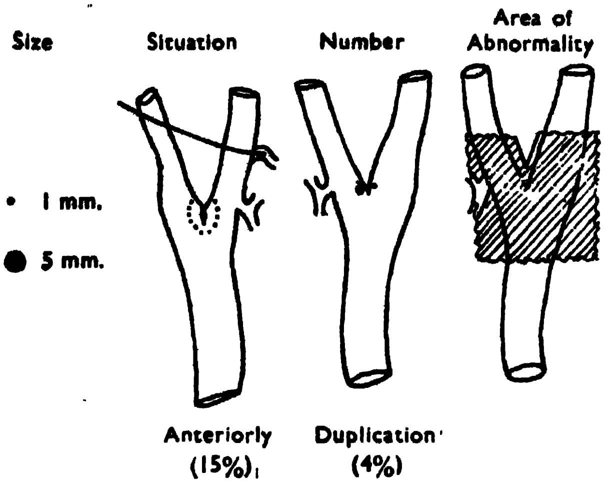

FIG. 3—DIAGRAMS SHOWING VARIATIONS IN SIZE, SITUATION, NUMBER AND AREA OF ABNORMALITY OF THE CAROTID BODY

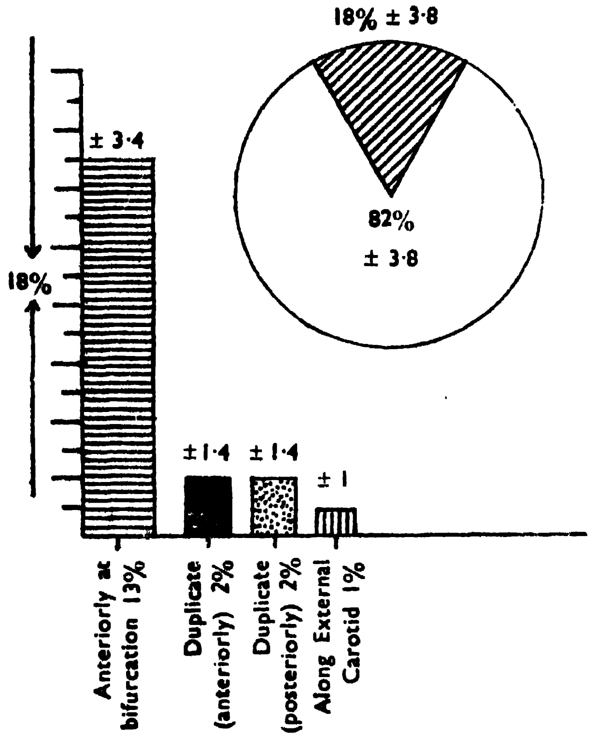

FIG. 4—SHOWING PERCENTAGE VARIATION OF THE SITUATION, NUMBER AND AREA OF ABNORMALITY OF THE CAROTID BODY

noted to be bilaterally symmetrical. Histology was constant.

Figs. 3 and 4 summarise the variations and the expected standard deviations. These variations have been confirmed at operation. Prof. Nakayama whom we had in our midst in January, 1964 also agreed that his experience was similar.

Very occasionally the glomus may be situated more deeply, partially embedded in the media of the vessel. Such glomera are liable to be missed at operation, particularly if they happen to be small.

Secondly, the operation being in status asthmaticus, one encounters more bleeding due to the engorged neck veins. Retraction of the overactive sternomastoid only provides a limited exposure.

RESULTS

Criteria of improvement were: (A) Subjective—Improvement in breathing ability. (B) Objective—(i) Complete disappearance of wheeze; (ii) Improved air entry (chest expansion of more than 1 inch); and (iii) Disappearance of cyanosis, if present.

It will be noted that only complete disappearance of wheeze was considered significant. If the slightest wheeze persisted result was charted as partial relief (P). At times air entry is not easy to judge in the noisy, gurgling chest of the asthmatic in status. We used expansion of the chest at the nipple line as our measure of air entry. Only a reading over 1 inch was considered significant.

The use of pulmonary function tests as an aid to assess improvement, was given up after initial trial, because the results were unreliable. Due to lack of facilities only ventilatory functions like F.E.V., M.B.C. and timed vital capacity were used. As is well accepted, these depend so much on the co-operation of the patient, which we found hard to elicit from these frightened, suffocating asthmatics in status.

The results are shown in Table 1.

It will be noted that in 20 patients out of 24, wheeze completely disappeared. In the remaining 4, it took a maximum of 12 hours to do so. All had significant subjective relief and improvement in air entry.

The pattern of relief is also noteworthy. No relief was obvious on injection of local anaesthetic, taking the incision or looping the common carotid. Relief began as soon as the adventitia was stripped and was best experienced by the patient on removal of the carotid body. Two of our patients had volunteered this information even before the incision was sutured.

DISCUSSION

Although the series is a small one, logical inferences, we feel, can be drawn as glomectomy has so far never failed to remit status asthmaticus.

On critical grounds, relief obtained could be due to:

(a) Late effect of drugs, already administered for the relief of asthma; (b) Premedication (pethidine and chlorpromazine); (c) "Psychotherapy"—

TABLE 1—SHOWING DETAILS OF THE CASES STUDIED

No.	Reg. No.	Name	Sex	Age	Duration		Drugs	Histology	Relief		
					Disease (years)	Attack (hours)			Subjective	Objective	
										Wheeze	Air entry
									OPERATION		
1	62/32439	L.L.	M	45	12	13	Ad. Am.	Positive	+	+	+
2	63/5194	D.B.	M	50	30	16	Ad. Am. Am.	Positive	+	P+ 12 hrs.	+
3	64/1167	P.R.	M	50	15	10	Ad. Am.	Positive	+	+	+
4	63/32347	J.R.	M	29	4	14	Ad. Am. Am.	Positive	+	+	+
5	64/33563	J.D.	M	35	13	16	Ad. Ad. Am.	Positive	+	+	+
6	63/32949	R.P.	M	25	9	12	Ad. Am.	Positive	+	+	+
7	62/35770	SHFM	M	26	14	24	Ad. Am. Am.	Positive	+	+	+
8	62/35853	H.R.	M	17	3	24	Ad. Am. Am.	Positive	+	+	+
9	62/38725	H.S.	M	35	8	26	Ad. Ad. Am. Am.	Positive	+	+	+
10	62/39536	Y.A.	M	40	3	48	Ad. Am. Pred.	Positive	+	P+ 4 hrs.	+
11	62/39118	P.M.M.	M	48	15	60	Ad. Am. Pred.	Positive	+	+	+
12	62/36856	S.M.S.	F	20	10	19	Ad. Am. Am.	Positive	+	+	+
13	62/37849	R.R.A.	F	40	12	14	Ad. Am.	Positive	+	+	+
14	62/37852	R D.	F	18	10	18	Ad. Am.	Positive	+	+	+
15	63/13801	P.D.	F	35	10	28	Ad. Am. Am.	Positive	+	+	+
16	62/246928	D.D.	F	28	14	14	Ad. Am.	Positive	+	+	+
17	63/2137	K.G.	F	17	4	20	Ad. Am. Am.	Positive	+	+	+
18	64/20275	M.P.	F	40	9	28	Am. Pred.	Positive	+	+	+
19	64/20278	N.C.	F	35	5	16	Ad. Am.	Positive	+	+	+
20	64/20271	M.P.	F	45	6	14	Ad. Am.	Positive	+	P+ 10 hrs.	+
21	63/30301	J.G.	F	18	12	36	Ad. Am. Pred.	Positive	+	P+ 6 hrs.	+
22	63/137329	C.G.	F	42	16	44	Ad. Am. Pred.	Positive	+	+	+
23	63/28573	S.B.	F	40	5	30	Ad. Am. Am.	Positive	+	+	+
24	62/36711	S.B.	F	42	10	24	Ad. Am.	Positive	+	+	+

Ad. : Adrenaline
Am. : Aminophylline
Pred. : Prednisolone
+ : Significant improvement

P+hrs. : Partial relief at the end of operation, complete relief indicated in hours

suggestion, coaxing, fear, etc. ; (d) Operation ; and (e) Spontaneous.

After having allowed six or more hours for subcutaneous adrenaline and intravenous aminophylline to act, it will be agreed upon that these drugs are unlikely to procure relief. Moreover, many of these cases were adrenaline-fast, as so many chronic asthmatics become, with passage of time.

Premedication did not produce any obvious relief and, in fact, some patients, who refused surgery after having received their premedication, continued to be in distress with status (there were 4 such patients, not included in this series).

Evaluation of the psychological aspect of the relief from operation is most difficult to assess. There is a significant functional overlay in all chronic asthmatics and this, we feel, is one of the major handicaps in assessing results of any therapy in asthma. It is true that a certain amount of fear, anxiety and expectation is associated with all surgical operations. On the other hand, the pattern of relief, as already pointed out, is such that the removal of the carotid body can be virtually linked with the waning of bronchospasm.

The relief obtained in 24 consecutive cases of asthma, who were in status ranging from 10 to 60 hours is probably not a mere coincidence. The argument of spontaneous relief in these patients is untenable. Five cases were failures of steroids—the steroids having been administered in high doses. One of them had benefited from steroids previously. There were others who had received incomplete treatment with steroids but we have not included them as failures of steroids. A comparative study of therapy with steroids and operation would be interesting.

SUMMARY

Twenty-four selected cases of status asthmaticus were operated upon as an emergency measure. All had initial trial with drugs. Only 5 had full treatment with steroids, unsuccessfully.

A standard procedure of unilateral glomectomy with stripping of the adventitia over a distance of 1 inch, under local anaesthesia, was used.

Twenty were completely relieved at the end of the operation. Four were partially relieved, but the relief became complete within 12 hours.

Variations in anatomy of the carotid body are described as an aid to improvement of technique.

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PERCUTANEOUS NEEDLE BIOPSY

A Useful Diagnostic Aid

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Histological examination of tissue obtained from an internal organ by a biopsy needle has been found to be useful in the diagnosis of various liver, kidney and respiratory diseases. It is often helpful when all usual bedside and laboratory procedures have failed to give a definite diagnosis. Needle biopsy done by a physician at the bedside with minimum appliances will help in the diagnosis of a large number of cases. Sometimes it obviates the necessity for an open operation, i.e., a thoracotomy. Various types of needles can be used for such a biopsy but the Vim-Silverman needle, because of its simplicity and easy manoeuvre, has become popular.

The Vim-Silverman needle consists of three parts, viz., a short trocar and a cannula which is introduced percutaneously to the organ to be biopsied. The trocar is removed and the tissue punched out by the introduction of a stylet split longitudinally, both halves of which tend to spring apart. The cannula is then advanced until the tips are both at level. The apparatus is rotated to break off the end of the biopsy and withdrawn. Suction is not necessary and the method has a high success rate. There are other types of needle available, viz., Abram's needle for pleural aspiration and biopsy, aspiration biopsy needle, etc. but the author found Vim-Silverman needle to be the most convenient.

The percutaneous needle biopsy is used in the following circumstances:

1. IN DISEASES OF THE LIVER

A specimen of liver tissue is obtained by the biopsy needle for diagnosis of the following liver diseases:

(a) Cirrhosis of the liver—When from the clinical picture the diagnosis is not obvious. In advanced liver diseases, i.e., presence of ascites, splenomegaly, jaundice, spider naevi, a biopsy is not necessary for diagnosis.

(b) Tumours of the liver—A primary or a secondary tumour can be definitely diagnosed by a liver biopsy. In case of secondary tumours the biopsy from nodules on the surface of the liver will yield more positive results.

(c) Granulomas of the liver such as sarcoidosis, brucellosis, tuberculosis, etc.

(d) Infections such as amoebiasis, syphilis, histoplasmosis, leptospirosis, etc.

(e) Metabolic diseases such as amyloidosis, glycogen storage disease.

(f) Congenital hepatic fibrosis.

(g) Hepatomegaly of unexplained aetiology.

Technique of liver biopsy—The method described by Sherlock (1963) has been followed. Any bleeding tendency with a prolonged prothrombin time should be corrected by injection of vitamin K, 10 mg. daily for 3 days. If the patient is jaundiced with a prolonged prothrombin time, the procedure should not be undertaken.

If ascites is present fluid should be tapped beforehand. A sedation with 0·2 g. sodium amytal is given half an hour before the procedure. The patient should lie on the left side with right side uppermost and the right arm placed behind the head. The skin is sterilised, and the skin and subcutaneous tissue are infiltrated with 2 per cent procaine solution up to the capsule of the liver, either through 8th, 9th or 10th intercostal space or subcostally when the liver is enlarged 3-4 finger breadths below the right costal margin. A small incision is made over the skin by a scalpel and the biopsy needle is introduced up to the substance of the liver. The trocar is removed and with the biopsy stylet a piece of liver tissue is obtained. In the intercostal approach the patient must be co-operative and should be able to hold his breath during the procedure. Following the biopsy the patient should lie in bed for 24 hours.

The following complications may occur:

1. Haemorrhage—Bleeding from the punctured site in liver into the peritoneum may occur occasionally.
2. Bile peritonitis from puncture of the bile duct or gallbladder.
3. Pleurisy and perihepatitis may occur in the intercostal approach which usually subside in 24 hours.

In expert hands it is rare to have complications. Gupta *et al.* (1964) reported 1,800 cases of liver biopsies and reported that in 39 per cent of their cases of obscure ascites a diagnosis could be made. In their series the clinical diagnosis was confirmed in 62 per cent of their cirrhosis cases.

2. IN DISEASES OF THE PLEURA

In cases of pleural effusion, tissue obtained from pleura by a Vim-Silverman needle may help in the diagnosis, as to the cause of effusion, which cannot be done by other means. In the presence of a large effusion the technique becomes rather simple. The biopsy helps in the diagnosis of:

(a) Tuberculous effusion.
(b) Malignant pleural effusion.
(c) Inflammatory effusion.
(d) Effusion due to other causes.

Technique of pleural biopsy—A sedative, such as 2 g. sodium amytal is given half an hour before the procedure. With the patient sitting the skin is sterilised and the skin and subcutaneous tissue up to the pleura are infiltrated with 2 per cent procaine solution. The needle is introduced posteriorly until fluid is obtained from the pleural space. The needle is slowly withdrawn till fluid just stops coming. This distance from the skin surface is measured and a clamp is placed in the biopsy needle up to that distance. The biopsy needle is introduced up to the pleura and a piece of pleural tissue is taken by the biopsy stylet. With experience, the pleura can be felt by the biopsy needle and proper tissue biopsy thus assured.

Defrancis *et al.* (1955) were the first to use the technique in six cases of pleural effusion and diagnosed two cases as tuberculosis by biopsy. The biopsy yields more positive results in cases of tuberculous effusion because the pleural involvement is diffuse there. Abrams in 1958 invented a needle which goes by his name by which both pleural aspiration and biopsy can be done at the same sitting. He established a positive diagnosis in 80 per cent of cases of pleural effusion. Pragni *et al.* (1962) in India diagnosed 47 per cent of their pleural effusions by using Abram's needle.

The pleural biopsy is most helpful in the diagnosis of tuberculous pleural effusions when the long-term antituberculosis treatment can be given with a definite diagnosis. The biopsy also can differentiate the effusion in cases of lung cancers to be of metastatic origin or of infectious origin.

Complications, such as chest pain, pleural shock, local haematoma may occur. The author observed in two cases of pleural biopsy done by Abram's needle large haematoma at the biopsy site on exploration.

3 IN DISEASES OF THE LUNGS

Quite frequently a lung lesion may not be diagnosed by conventional methods, such as x-ray and sputum examination. In these circumstances a needle biopsy of lung tissue may be of invaluable help. Though the blind biopsy of lung tissue may not be as innocuous as pleural biopsy, still in experienced hands with proper selection of cases this can be done with minimum of complications. The biopsy is helpful in the diagnosis of:

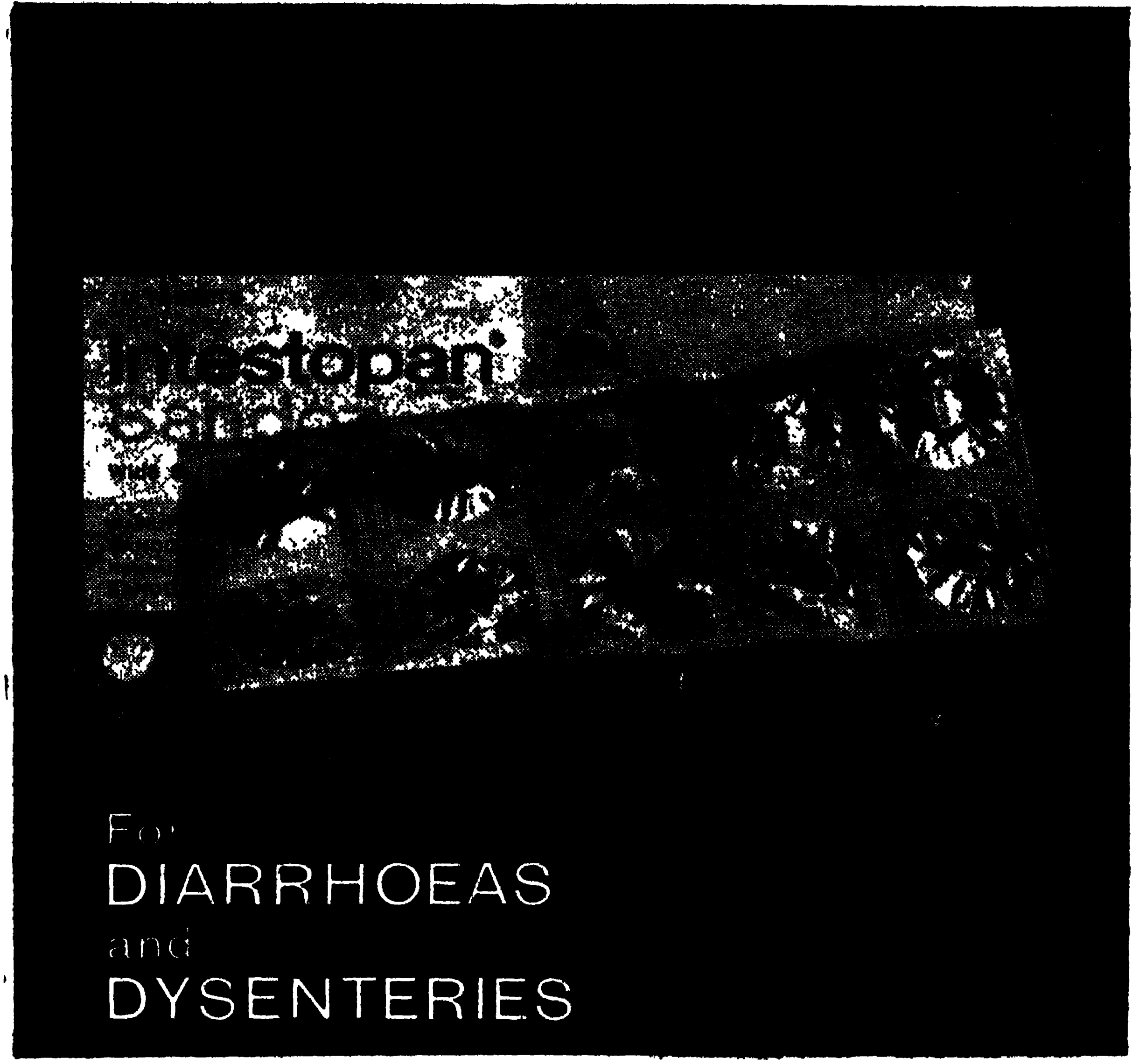
(a) Diffuse pulmonary lesions, viz., interstitial fibrosis, sarcoidosis, metastatic carcinoma of lungs.

(b) In lung cancers where the lesion is located peripherally and is not visualised by a bronchoscope.

(c) Any lung lesion of unexplained actiology.

Technique of lung biopsy—Sabour *et al.* (1960) method is followed. Selection and preparation of the patient: (1) Patients with pleural effusion should have the fluid removed before biopsy. (2) Patients must be co-operative, because if he breathes with the needle in the lungs a longitudinal rent will be produced. (3) Biopsy should not be performed if facilities for blood transfusion are not available. (4) A mild sedative, such as sodium amytal is given half an our beforehand. As cooperation of the patient is necessary stronger sedatives should not be given. (5) Radiograph is essential to exclude pulsating shadows. A P.A. and a lateral view are necessary to exactly localise the lesion.

Procedure—The intercostal space overlying the lesion is used for puncture as indicated by radiography. If there is clinical dullness the site of maximum dullness is chosen. The patient lies supine with the side on which the biopsy is to be done at the edge of the bed. A firm pillow is placed under that side to raise it and open the intercostal spaces as for artificial pneumothorax. After preliminary cleansing, the skin is anesthetised



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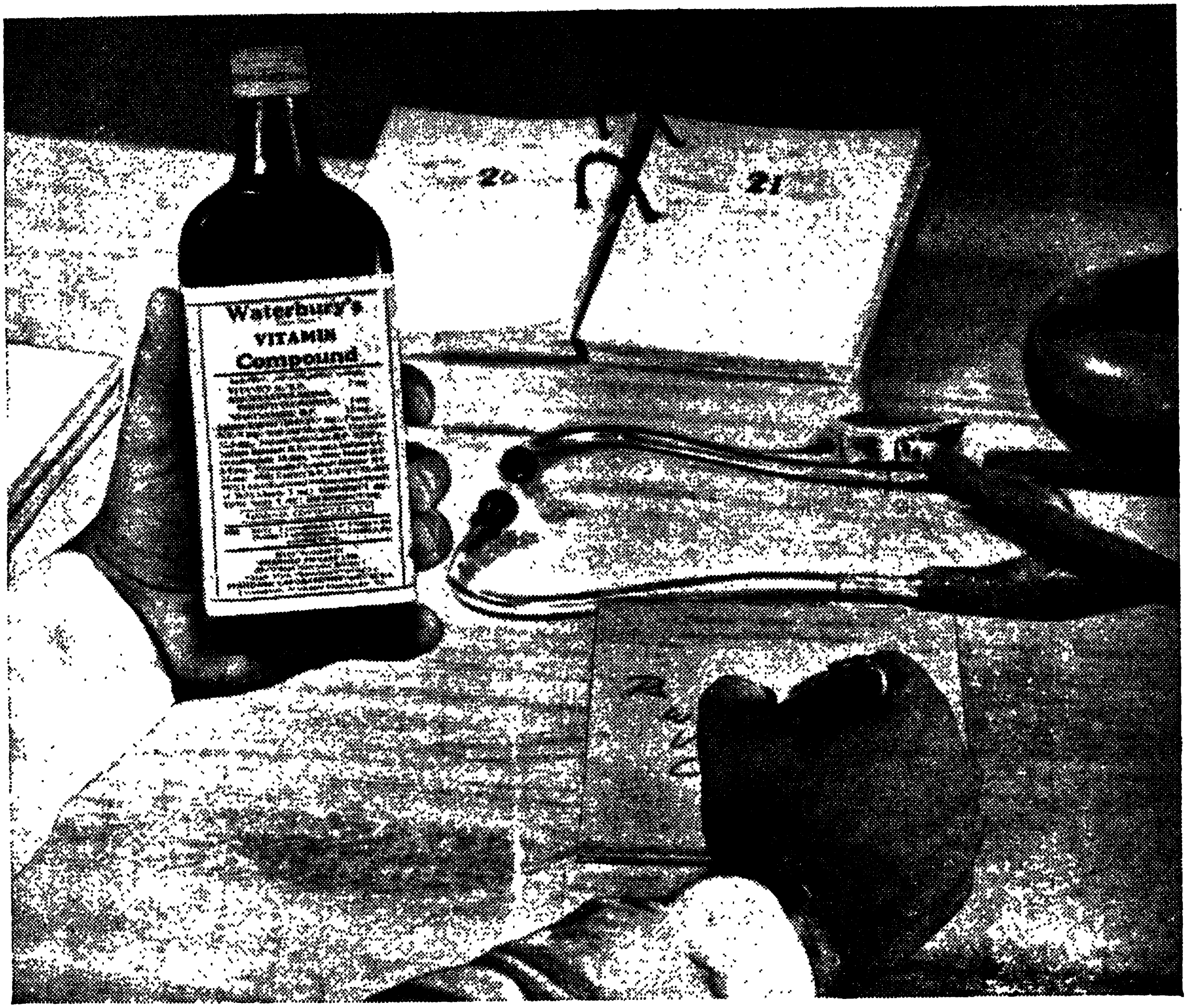

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with 2 per cent procaine solution. A Vim-Silverman needle is inserted quickly and lung tissue withdrawn by means of biopsy stylet.

Lung biopsy was first performed by Fazio *et al.* (1955). In 9 of their cases 5 were diagnosed to be carcinoma of the lung. Sabour *et al.* (*loc. cit.*) performed lung biopsy in all kinds of undiagnosed lung lesions totalling 137 cases. The yield of positive diagnosis was much higher in their series. Lung biopsy is most helpful in the diagnosis of carcinoma of lung and makes a thoracotomy unnecessary for diagnosis.

Complications, such as haemoptysis and pneumothorax may occur occasionally.

4. In Diseases of the Peritoneum

A peritoneal biopsy has been found useful in the diagnosis of different types of ascites:

(a) Tuberculous peritonitis.
(b) Malignant peritonitis.
(c) Cirrhosis of the liver.
(d) Any unexplained ascites.

Technique—The method of Donohoe *et al.* (1957) is followed. After mild sedation the patient is placed in the sitting position and an abdominal binder is applied. The site of puncture is between the umbilicus and the symphysis pubis. After local anaesthesia the Vim-Silverman needle is introduced into the peritoneal cavity. The trocar is withdrawn and fluid flows out. The needle is withdrawn till fluid just stops coming out and trickles in drops. This places the edge of the needle at the level of the parietal peritoneum. Biopsy stylet is then introduced into the cannula till resistance is felt and the patient is asked to increase the intra-abdominal pressure. The needle is then rotated through an angle of 360 degress and biopsy material obtained by withdrawing the needle.

The proceedure is simple but it is often difficult to get adequate peritoneal specimen for histological examination. Mehrotra *et al.* (1964) could diagnose 33 per cent of cases of tuberculous peritonitis by peritoneal biopsy. It strongly suggested tuberculosis in another 20 per cent of cases. The biopsy also helps in the diagnosis of tuberculous peritonitis in the presence of cirrhosis of liver.

5. In Diseases of the Kidney

A kidney biopsy is indicated in the diagnosis of any diffuse renal disease which cannot be diagnosed by the usual clinical procedures. It is of particular value in:

(a) Differential diagnosis of unsuspected inflammatory and infectious diseases of the kidney.
(b) Collagen diseases.
(c) Nephrotic syndrome.
(d) Patients with proteinuria.
(e) Follow-up of patients of lupus nephritis when treated with steroids.

Contraindications of kidney biopsy: (a) Uncooperative patients, (b) single kidney, (c) terminal renal failure, (d) abnormalities of coagulation.

Technique of Muehrcke *et al.* is followed. At first the kidney is located by a straight film of the abdomen or I.V. pyelogram. A point is taken in the lower outer pole of the right kidney by measuring its distance from the iliac crest and vertebral border. This point is about half an inch below the right 12th rib and three inches from the vertebral border. The skin over this area is infiltrated with 2 per cent procaine solution, as also the subcutaneous tissue using a 6 inch 20-gauge needle which is passed downwards and obliquely. The back muscles and lumbar fascia give a characteristic resistance and when this has been overcome the needle is pushed a little further until it appears to swing freely with respiration. The depth of the needle from the skin is measured. This depth from the needle is taken in the Vim-Silverman needle which is introduced through the skin in a rotatory fashion until a sudden 'give' is felt due to piercing of kidney tissue, and the needle swings freely with respiration. Patient is now asked to hold his breath. Trocar is removed and the biopsy stylet is entered to its full length. The cannula is advanced and the whole needle is rotated 180 degrees so as to cut a cylinder of kidney tissue. The needle is withdrawn and biopsy tissue preserved in formalin.

Complications including microscopic haematuria, loin pain, fainting attacks during the procedure may occur occasionally.

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PLEURAL EFFUSION AND SUPERIOR VENA CAVAL SYNDROME IN HODGKIN'S DISEASE

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Pleural effusion is frequently encountered in private as well as hospital practice. It is also an infrequent complication of Hodgkin's sarcoma.

Hodgkin's disease affects the lymphoid as well as non-lymphoid organs. Liver has been found involved in 38 per cent of cases and spleen in 80 per cent. Of 63 cases of Hodgkin's granuloma, Jackson and Parker (1944, 1945) found spleen to be affected in 47 instances, liver in 31 and bones in 35. In this series they found mediastinal lymph nodes to be diseased in 59 instances In 9 cases, the mediastinal lymph nodes were found to be the primary sites. In 32 cases of Hodgkin's sarcoma, the same authors found the mediastinal lymph nodes involved 14 times. In many instances the process was confined to one group of lymph nodes only. Thus in 19 of 77 cases studied by Kasbach and McAlipen (1848), none showed involvement of peripheral nodes. This observation is of importance because negative finding in one node does not exclude the presence of the disease in other nodes.

Hodgkin's disease primarily and predominantly affects the lymph nodes of the middle mediastinum.

The lungs are affected by Hodgkin's disease with comparative frequency. As a rule, the lungs are invaded from the mediastinal lymph nodes. Cases are on record where Hodgkin's disease was presumed to have originated primarily in the lungs.

The pleural leaflets are usually reached from the mediastinal lymph nodes, although instances have been reported where a granulomatous pleuritis was present without the involvement of mediastinal lymph nodes. French clinicians speak of a predominantly pleural Hodgkin's disease. Ten out of 63 cases of Hodgkin's granuloma studied by Jackson and Parker (*loc. cit.*) showed involvement of the pleura.

Whenever the pleura becomes affected, it is accompanied by unilateral or bilateral effusion, which closely resembles the effusion produced by carcinoma. The fluid is usually clear, straw coloured and rich in fibrin. A haemorrhagic exudate has been observed in a few instances. A chylothorax described by Edsal (1905) was attributed to compression of the thoracic duct or possibly to concomitant tuberculosis.

In cases where the aetiology of an effusion is obscure, the possibility of its being caused by Hodgkin's disease should be kept in mind.

Other manifestations of Hodgkin's disease are frequency of micturition and dysuria, neurological symptoms, jaundice, ascites, etc.

Hodgkin's disease has been classified into three types, such as paragranuloma, granuloma and sarcoma.

Hodgkin's paragranuloma is characterised by the appearance of superficial lymph nodes which are firm, painless and outwardly normal, but microscopically infiltration with lymphocytes and Sternberg-Reed cells is seen.

The most frequently encountered Hodgkin's granuloma is a conglomeration of cells consisting of Dorothy-Reed cells, lymphocytes, neutrophils, eosinophils, plasma cells and fibroblasts with areas of necrosis. There may be associated enlargement of spleen.

Hodgkin's sarcoma is really a reticular cell sarcoma arising during the course of Hodgkin's disease. Lymphoid tissue is replaced by a tumour composed almost entirely of reticulum cells.

CASE REPORT

A male patient, aged 70 years, was admitted to the hospital complaining of (1) dysuria for 1 year ; (2) oedema of feet for 8 months ; (3) breathlessness for 1 month ; and (4) cough with expectoration for 1 month.

The patient complained that his breathlessness had increased since 7 to 8 days. He felt dyspnoeic on walking a few steps, and felt better in orthopnoeic position. Oedema of feet developed gradually, and there was pitting on pressure. He used to cough up a little purulent expectoration.

There was no history of hypertension, coronary insufficiency, dyspnoea, jaundice, swelling of neck, haemoptysis, etc. The patient used to smoke 25 *bidis* daily and drink alcohol for the last 40 to 45 years.

On general examination the patient was found asthenic. The pulse was 108/min., respiration 30/min. and thoracic in type ; B.P. 126/64 mm. of Hg ; jugular venous pulse + on both sides ; scaling of skin of fingers was present.

Lymph glands: A few were palpable in the neck. They were firm, discrete and not tender. In the axilla, they were not palpable. Inguinal lymph glands were palpable.

Prominent veins were seen on the chest and abdomen, the flow being from above downwards, indicating superior venacaval block.

Respiratory system: Chest movement was diminished on the left. Trachea was shifted to the right. T.V.F. was diminished and there was dull note, all over the left side. Air entry and vocal resonance were also less on the left side. These suggested pleural effusion on the left side.

Alimentary system: Liver was three fingers palpable, smooth, firm and tender on pressure. Spleen was five fingers palpable, smooth and firm.

Other systems: Normal.

Investigations—Blood: Hb.—9 g. per cent; W.B.C.—10,200/c.mm. with polymorphs 55 per cent, lymphocytes 40 per cent and monocytes 5 per cent. E.S.R.—90 mm./hour.

Urine showed absence of albumin.

Sputum examination showed pus cells, gram-positive cocci and gram-negative diplococci. Culture and sensitivity report—*K. pneumoniae* grown, resistant to all.

Pleural aspiration: Total proteins 3·5 g. Total cells 420/c.mm. Differential count: Polymorphs 20 per cent, lymphocytes 80 per cent. Smear—Squamous epithelial cells+; Neoplastic cells—nil.

Fluoroscopy showed pleural effusion on left side of chest. Skiagram was confirmatory.

E.C.G. showed abnormal T-waves.

Bone marrow showed erythroid, myeloid and megakaryocyte series (normal). Dorothy-Reed-Sternberg cells seen.

Pleural biopsy showed neoplastic cells having big vesicular and prominent nucleus, arranged as solid alveoli in a few areas. The cytoplasm was pink and borders were indistinct.

The two possibilities considered by the pathologist were Hodgkin's sarcoma, and metastatic carcinoma having site unknown.

Lymph node biopsy showed Hodgkin's paragranuloma.

Treatment—The patient was treated with prednisolone tablets. The liver receded and was just palpable, and spleen receded to three fingers. Patient was less breathless. He had no effusion afterwards, and felt better.

DISCUSSION

The patient complained of dysuria, breathlessness and cough with expectoration. He showed signs of superior vena caval block; a few firm and discrete lymph nodes were present; and liver and spleen were enlarged three and five fingers respectively.

The diagnosis of Hodgkin's disease was obvious from clinical features. The overall picture had two interesting features. One is the occurrence of Hodgkin's disease at this late age, the disease being common at the age of 30 to 35 years, while it is uncommon at the age of 70. The second feature is the involvement of pleura along with sarcomatous change. Coexistence of low grade and high grade malignant Hodgkin's disease is known, but Hodgkin's sarcoma of the pleura is a rare entity.

The patient was treated with prednisolone tablets. Both the liver and spleen gradually receded. The liver was no longer palpable and the spleen was three fingers palpable 18 days after starting treatment. The patient felt better and he had no pleural effusion thereafter.

SUMMARY

A case of Hodgkin's disease is presented with Hodgkin's sarcoma of the pleura, superior venacaval syndrome and pleural effusion.

Sarcomatous involvement of pleura along with pleural effusion is a rare feature although low grade and high grade type of malignancy may coexist in Hodgkin's disease.

Prednisolone therapy produced symptomatic relief with regression in size of liver and spleen and disappearance of pleural effusion.

ACKNOWLEDGMENT

The authors are grateful to the Dean, Topiwala National Medical College and Nair Hospital, for permission to report this case.

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THE SYNDROME OF PTOSIS, GENERALISED MUSCULAR WEAKNESS AND MARKED FASCICULATIONS OF CALF MUSCLES DUE TO INSECT BITE

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The venenating arthropods which injure human beings with bites, stings and contact include centepedes, scorpions, spiders, ticks, bees, wasps, ants, beetles and the caterpillars of moths and butterflies (Cecil and Loeb, 1964) and scorpion-like organism with six spots on the body mainly found in this locality. Out of these, only scorpions, spiders, ticks and the local variety of scorpion-like organism produce neurotoxicity due to their bites. Scorpion bite results in convulsions and encephalitis-like features and death. Black widow spiders bite causes generalised muscular spasm specially of abdominal muscles, convulsions and neuritis; tick causes tick paralysis characterised by flaccid paralysis of extremities and bulbar muscles with subjective sensory disturbance. Local six-spotted scorpion bite results in fatal encephalitis. The cases described below did not resemble any of these and yet they resembled each other so closely that those who had not seen such cases before, when first encountering this condition in 1963 were puzzled to fit it with any known neurological disorder, while those with experience gave the spot diagnosis of insect bite. Unfortunately, insects are not recognised because bites occur at night.

CASE REPORTS

Case 1—Male, 26 years, came to hospital in July 1963 with history of insect bite on 12th July at 3 o'clock in the morning. He was bitten by an insect in his left ear. Next morning he felt pain in left ear, tiredness and drooping of eyelids. On examination, he was conscious with pulse rate 75 per minute, temperature 98°F., B.P. 130/82 mm. Hg. Systems other than the central nervous were normal.

C.N.S.: Generalised muscular fasciculations but most marked in both calf muscles and also in tongue, were noticed. Bilateral paralysis of levator palpebrae superioris, partial weakness of facial muscles, diminished in both upper and lower limbs, more marked in proximal than in distal muscles; all deep reflexes present, normal, plantar reflex—flexor, and no sensory loss except at the site of insect bite in an area of two mm. which was black and anaesthetic.

Investigations: Total W.B.C. 6500 per cmm. with polymorphs 75 per cent. E.S.R. 20 mm./1st hour, C.S.F.—protein 34 mg. per cent, sugar 70 mg. per cent, chloride 730 mg. per cent, cells 0-2.

Muscle biopsy normal. S.G.O.T.—42 units. E.C.G.—normal. The patient was treated with intravenous cortisone and vitamins B_1 and B_{12} with dramatic result, recovering completely in six days.

Case 2—Male, 52 years, was bitten on the chest at 11 P.M. The patient slept till 3 A.M. then felt pain at the site of bite and jaw.

Generalised fasciculations were seen including tongue but was much more marked in calf muscles. On examination, cranial nerves showed bilateral ptosis. Internal ocular muscles were intact. Weakness of masseter, temporalis, pterygoides, and facial muscles were detected and dysphagia, more with liquids than solids, and dysarthria were present. Power diminished in limbs, more marked in proximal group of muscles. Reflexes were present, plantar—flexor. No sensory changes were detected.

Investigations: Total W.B.C. 7800 per c.mm., Hb. 94 per cent, urine normal. E.S.R. 15 mm./ 1st hour, C.S.F.—protein 20 mg. per unit; chloride 700 mg. per cent, sugar 50 mg. per cent.; cells 1·2 per field. S.G.O.T.—32 units; E.C.G.—normal. Muscle biopsy—normal. The patient improved with cortisone therapy.

Case 3—Male, 48 years, had a bite on right ankle and developed almost identical clinical features as Case 2, except the fasciculations which were only seen in the calf muscles and improved with cortisone.

Case 4—Male, 56 years, came with insect bite at night, and the patient started feeling weakness and tiredness in the morning. On examination, fasciculations, only in calf muscles, and ptosis were present; but other ocular muscles were intact. Other cranial nerves were intact; the limb weakness was generalised and was more marked in proximal muscles. Reflexes were present. Plantar reflex was flexor. No sensory changes were detected.

Investigations including muscle biopsy were within normal limits. The patient responded very well to I.V. cortisone and recovered in 4 days.

DISCUSSION

The cases were encountered mostly in the rainy season, a time notorious for bites in this locality. The sites of bites were variable showing no predilection for any part. The interval between bite and production of symptoms varied from three to four hours, and symptoms were generalised, indicating blood-borne dissemination. Why there were predilection for ptosis and fasciculations most marked in calf muscles could not be explained. The clinical features apparently resembled myasthenia gravis but there was no increased fatiguability of muscles and there was no variability of signs. The site of action of toxins whether on anterior horn cells, nerve roots or fibres or on motor end-plates could not be inferred. Fasciculations do not occur when cells are rapidly injured or destroyed as in acute anterior poliomyelitis (Brain, 1964); fasciculations occur either due to chronic degeneration of anterior horn cells or it may occur sometimes in peripheral nerve lesion, in which cases discharges appear to be originating at some point in the terminal arborisations of the motor unit by a motor akenion reflex (Morgan Campbell and Dickinson, 1964). Here the disease process was acute and all improved within six days. The sensory symptoms were conspicuous by their absence except at the site of bite which might be due to excessive concentration of toxins. The excessive fasciculations indicate that the toxins might contain anti-cholinesterase-like substances (Samson Wright, 1961). The response to cortisone was marvellous in all cases.

SUMMARY

Four cases of insect bite leading to generalised muscular weakness, ptosis and fasciculation most marked in calf muscles have been described. All the patients responded to cortisone therapy.

ACKNOWLEDGMENT

The author is thankful to Dr. M. Das, Professor of Medicine and Head of the Department of Medicine, Patna Medical College Hospital, for encouragement and advice, and to Dr. C. D. Singh, who referred the first case to him.

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SUBCONJUNCTIVAL SALINE AS TEST AND TREATMENT FOR OCULAR MALINGERING

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A patient whose fundus is normal and pupil normal in size, shape and in reaction to light, rarely complains of sudden loss of vision in one or both eyes. On being tested even perception of light is found to be absent in the affected eye. These are problem cases ; because such sudden and complete loss of vision in a patient with normal fundus and normal pupil can only be seen if there is some lesion of sudden onset in the occipital cortex round about the calcarine fissures—trauma, vascular lesion or some vasospasm of retinal blood vessels, or rarely in cases of unilateral retrobulbar neuritis. Where there is vasospasm, the loss of vision is transient and in retrobulbar neuritis the pupillary reaction is unsustained.

When we have ruled out these organic lesions, the diagnosis of malingering remains. The malingerers are usually young persons more commonly females in the age group of 15 to 30 years. On taking a detailed history, one can find out a cause for which the patient complains of loss of vision.

The test with a low convex glass in front of the blind eye and +20D in front of the good eye, the diplopia test with prism confirms that the patient is malingering.

We came across four such patients of whom two who were malingering for both eyes and two for one eye. After carefully taking the history, organic causes which might have given rise to this sudden loss of vision were excluded, and malingering was apparently confirmed by diplopia test.

The patient was asked to lie down. No local anaesthesia was put in the affected eye and 0·25 ml. of normal saline was injected subconjunctivally in the upper half of the affected eye as near to the limbus as possible. As local anaesthesia was added, this injection produced a lot of pain. It was then explained to the patient that more of it will be injected, if the patient failed to regain vision. To our utter surprise, we found that all the four patients reported about the recovery of vision in one or both the affected eyes, just after this injection.

These four cases are reported in this paper. All the four patients complained of sudden and complete loss of vision in one or both eyes. They had normal C.N.S., normal fundus and the pupil also was normal in size and reaction to light.

CASE REPORTS

Case 1—A married girl, aged 18 years, was brought to the Ophthalmic O.P.D. with history of sudden loss of vision in both eyes. She kept her eyes closed and was walking with the help of her two relations. The history was that she was staying with her husband. As her grandmother-in-law had fallen ill in the village, the girl was sent there three days ago. There, she had to do lots of work. She complained of complete and sudden loss of vision in both eyes one day back. Fundus and pupil—N.A.D. Vision : B.E.—No perception of light present. After 0·25 ml. of subconjunctival saline administration in R.E., she got her vision back in both eyes within a few minutes and she could now read 6/9 with both eyes.

Case 2—A man, aged 20 years, attended the Ophthalmic O.P.D. with complaint of sudden loss of vision in B.E. of 8 hours' duration. Patient's brother had a shop and the patient attended it during the absence of his brother who went out four days ago. The brother returned back unexpectedly and wanted to check the shop accounts. Since that time the patient complained of sudden loss of vision in both eyes. On examination it was found that fundi and pupils were normal. As regards vision, only perception of light was present. Patient could read 6/6 with both the eyes, after subconjunctival administration of 0·25 ml. of normal saline in both the eyes.

Case 3—A girl, aged 18 years, with complaint of sudden loss of vision in right eye attended Ophthalmic O.P.D. She had been recently married and had gone to stay in her husband's village home with her husband. Her husband later had come down to Benaras to continue his studies and she went to her father's place. Three days back she came to Benaras to stay with her sister, and her husband did not know it. According to her sister, the patient was alright till the previous evening, when she complained of sudden loss of vision in the right eye.

Right eye : Fundus and pupil were normal. Vision—perception of light absent. 0·25 ml. of normal saline was injected subconjunctivally in her right eye, and just within a few minutes she could read 6/9 with her right eye.

Case 4—A woman, aged 28 years, came to O.P.D. with sudden loss of vision in the left eye of one day's duration. The history was that she had quarrelled with her mother-in-law and the husband had taken the side of his mother. Fundus and pupil were normal. Vision in right eye 6/5 ; left eye—PL absent.

0·25 ml. of normal saline was injected subconjunctivally in left eye, and just then she could read 6/12.

SUMMARY

0·25 ml. of normal saline when given subconjunctivally, to four malingering patients complaining of sudden loss of vision in one or both eyes brought back the vision to normal within a few minutes. This can be used either as a test or treatment for malingering patients, who complain of sudden loss of vision.

THYROTOXIC EXOPHTHALMOS WITH OPHTHALMOPLEGIA AND OCULAR MYASTHENIA GRAVIS

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An exophthalmos associated with endocrine dysfunction, has been a problem to clinicians all over the world. Its behaviour is so incalculable that often it is not possible to label a case to a particular group, viz., thyrotoxic exophthalmos and thyrotropic exophthalmos. An associated ophthalmoplegia of varying degree and multifarious lid signs further complicate the issue. Still annoying is the response of an eye in a particular individual to any state of thyroid function, from normal to hypo- and hyperthyroidism. An occassional association of myopathies and rarely myasthenia gravis makes the problem worse.

CASE REPORT

H., male, aged 24 years, was admitted in the M. Y. Hospital on 3-8-64. He complained of palpitation, restlessness, increased appetite, occasional loose motions, a feeling of warmth all over the body, bulging of the eyes with difficulty in reading and writing, and inability to move the eyes and close the lids—for the last 1 to 1½ years. He gave history of diplopia and ptosis of one or both the eyes, with remission and relapses for the last 12-15 years. He was married and had one issue. He smoked 10-12 cigarettes per day. There was no history of venereal disease. There was absence of weakness in any other part of the body. He was a clerk and experienced difficulty in carrying out his work efficiently.

On examination, the patient was thinly built, weighing 105 lb., the weight being constant for the last 5-7 years. The pulse rate was 105/min. and the B.P. 150/70 mm.Hg. There was fullness in the region of the thyroid, without obvious swelling, the tongue and hands displayed coarse tremors. All other systems showed no abnormality of any kind.

Investigations—The R.B.C. count, total and differential counts of W.B.C., E.S.R., blood sugar and blood cholesterol estimations and urine report showed no abnormality.

V.D.R.L. test—negative.

B.M.R.—positive 57.

Fluoroscopy showed enlargement of the left ventricle.

E.C.G. showed sinus tachycardia within normal limits.

X-ray chest and orbit showed no abnormality.

OCULAR FINDINGS (BEFORE PROSTIGMINE TEST):

Appearance: A fixed look with an expressionless face and proptosis.

Lids: The right lid was smooth and drooping (Fig. 1) with negligible movement in the upward direction. The left lid showed slight retraction with very little movement. The patient was unable to close the lids.

Ocular movements: Almost complete immobility of the globe, having not more than 1-2 mm. of the movement, only in right lateral gaze.

Pupillary reflexes: Brisk reaction to direct and consensual light reflex. Accommodation reflex was normal.

Other findings: Proptosis reducible; no chemosis of the conjunctiva; cornea was clear. The anterior chamber was normal, showing physiological cupping.

OCULAR FINDINGS (AFTER PROSTIGMINE TEST):

Appearance—Typical staring and frightened look of thyrotoxicosis; no change in the expression of the face.

Lids: The upper lids were well retracted exposing more than 3-4 mm. of sclera above the cornea (Fig. 2). The lid had gained the power of movement.

Ocular movements: An appreciable improvement in the movement of the globe to the extent of 3-4 mm., more so in the right gaze, appeared after prostigmine test.

Pupillary reflex: There was no change in the pupillary reaction.

Other findings: There was no reduction in the amount of proptosis.

PROSTIGMINE TEST:

1 mg. of prostigmine was injected intramuscularly. The improvement in the lid movement was noticed in 10-20 minutes (Figs. 3 and 4) and full effect apeared in an hour (Fig. 2).

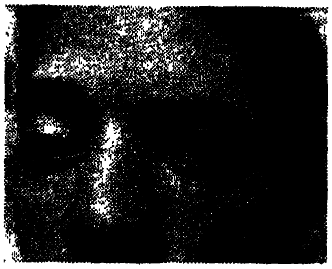

Fig. 1—Showing Ptosis of Right Lid and Left Lid Well Retracted (Before Prostigmine Test)

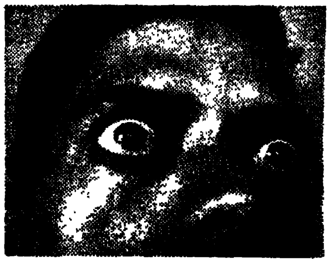

Fig. 2—Showing Well Retracted Upper Lids (30 Minutes after Prostigmine Injection)

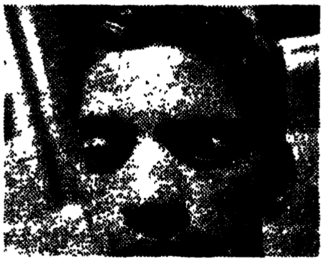

Fig. 3—Showing Almost No Retraction of Upper Lids (10 Minutes after Prostigmine Injection)

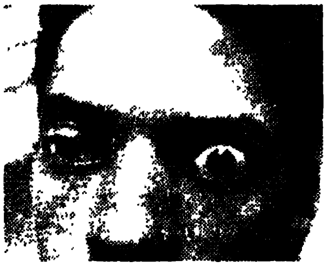

Fig. 4—Showing Increased Retraction of Upper Lids (20 Minutes after Prostigmine Injection)

Comments

An exophthalmos is a constant feature of Grave's disease, and its definite occurrence with thyrotropic disorder is unquestionable.

Hatch (1952) reported its occurrence with myasthenia gravis alone without hyperthyroidism and demonstrated its relief with neostigmine injection.

Grob (1953) observed four cases who exhibited exophthalmos seemingly as a part of myasthenia gravis In the present case, prostigmine test failed to show any relief of exophthalmos. An absence of conjunctival chemosis, with its reducibility on pressure and free mobility on traction test, excludes thyrotropic exophthalmos. The general symptoms of thyrotoxicosis with raised B.M.R. are sufficient to lebel it as a case of thyrotoxic exophthalmos.

Grob (*loc. cit.*) concluded that when localised ocular myasthenia gravis becomes generalised, it usually does so within the first year of the disease. The present case complained of ptosis of one or the other eye with diplopia for the last 12-15 years.

The smooth face, with a myasthenic snarl on smiling, was well observed in the present case. Mattis (1941) reported that patients were relieved somewhat on medication, although a few showed but little improvement in the status of facial involvement. Prostigmine test failed to show any improvement in the facial expression in our case.

Duke-Elder (1952) states that ptosis of one or both eyes is the first symptom in a large number of myasthenic cases, and this becomes evident eventually in 95 per cent of all patients.

The case presented here complained of drooping of one or both eyelids, with remissions and relapses, for the last 15 years. After prostigmine test both the lids retracted well away from the cornea showing a typical lid retraction which is found in exophthalmos due to Grave's disease (Fig. 2).

The pupillary reactions were normal, before and after prostigmine test. Mattis (*loc. cit.*) observed normal pupillary reaction in his series, although in a few cases they were occasionally sluggish.

The association of the myasthenia gravis with thyrotoxicosis is not so rare. Levy *et al.* (1951) in presenting five cases stressed that this combination is not rare, and may be easily overlooked or misinterpreted. Ophthalmoplegia occurs in almost all cases of myasthenia gravis, (Brain, 1962; Mattis, *loc. cit.*). Rundle and Wilson (1944) stressed the high incidence of ophthalmoplegia in Grave's disease. Mulvany and Mulvany (1943-44) stated that thyrotoxicosis caused a generalised myasthenia in which the more highly specialised eye muscles were the first to suffer. Brain (*loc. cit.*) states that exophthalmic goitre and myasthenia gravis may coexist in the same patient, in which case, thyroidectomy may not benefit the myasthenia; but there is also a thyrotoxic myasthenic condition which responds to neostigmine and is relieved by thyroidectomy.

The present case showed a marked improvement in the movement of the lids, but only an appreciable improvement in the movement of the globe, after prostigmine injection.

Summary and Conclusion

A case of thyrotoxic exophthalmos associated with myasthenia gravis of the ocular type has been described. Such association though not very common should be thought of especially if there is a combination of an expressionless face with drooping eyelids, with typical staring and frightened look of thyrotoxicosis. A routine prostigmin test in such cases is indicated. The relationship between the two diseases and their diagnosis have been discussed.

Acknowledgment

We are grateful to the Dean, M. G. M. Medical College, and Superintendent, M. Y. Hospital, Indore, for permission to report this case. We are also thankful to Dr. B. K. Dhir, Professor of Ophthalmology, and Dr. Akbar Ali, Professor of Medicine, for their criticism and suggestions.

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**JOURNAL OF THE
INDIAN MEDICAL ASSOCIATION**

CALCUTTA, NOVEMBER 1, 1965

THE PROBLEM OF ASTHMA

Elsewhere in this issue of the Journal will be found a summary of the proceedings of the World Asthma Conference[1] held in Eastbourne from 23rd to 26th March, 1965. In a foreward to the transactions of the Conference, Williams[2] has rightly pointed out that "this intractable disease puzzled doctors and tormented patients". Pearson[3] in his introductory address described asthma as "a condition about which we know a great deal but understand relatively little". In spite of the enormous volume of literature that has accummulated during the last few decades about respiratory allergy in general and asthma in particular, many problems pertaining to the condition have remained unsolved. It is not known whether asthma has a single pathogenesis or whether it is a syndrome due to various causes ultimately causing the same complex of symptoms.

The World Asthma Conference discussed the disease from several angles, medical, scientific and social. The natural history of the disease, its incidence and aetiology in countries like India, the changes that are seen post mortem, its influence on pulmonary efficiency, the fundamental mechanisms underlying its clinical manifestations, its psychological aspects, welfare and rehabilitation of those who are chronically disabled, and present-day methods adopted for management of the asthmatic patients, were considered and discussed in great detail. Sharp differences of opinion were expressed in regard to many of the aspects which came up for consideration. The main outcome of the Conference was the realisation that our understanding of the problem of asthma leaves much to be desired. The disease, no doubt, as Williams[2] has stated is a "reproach to the sciences of medicine". The Conference has no doubt made a valuable contribution in drawing the attention of not only the medical profession but also the general public to the importance of the subject. It has really helped in stimulating considerable amount of interest in the subject. It is hoped that more intensive efforts will be made to solve many of the problems pertaining to asthma and enable the members of the medical profession to make a rational approach to the management of the disease.

By far the most fruitful studies made during recent years have been on the fundamental problems connected with clinical immunology. The discovery of antihistaminics is a case in point. It will not be out of place to consider in this context, what is meant by the word allergy and allergic state. Symptoms in allergic diseases are produced as a result of tissue reaction based on antigen-antibody mechanism[4]. Antibodies produced as a result of contact with antigen are fixed to the cells which in consequence become sensitised. Further contact with the same antigen probably initiates an enzymatic process and a proteolytic enzyme is liberated from the cell. By the action of such enzymes on specific cells, histamine or histamine-like substances are liberated[4].

The relationship between histamine and clinical allergy is stressed by the fact that in allergic individuals the injection of a chemical histamine liberator (1935-L)[5] produces the usual spontaneous clinical symptoms like urticaria, asthma, etc., and that refractoriness of the histamine liberator is paralleled by clinical improvement in the occurrence of symptoms.

Most of the theories put forward to explain the basic mechanisms produced in clinical allergy has ignored the host or tissue factor, as attention has been concentrated on the antigen-antibody reaction. The tissue factor may be an enzyme mechanism, the disruption or natural exhaustion of which takes away the inhibitory action responsible for the production of histamine or histamine-like substances like seratonin, heparin, SRS-A, etc. Serafini[6] has observed that in bronchial asthma, besides the well known reagenic mechanism, the mechanism correlated with the presence of autoantibodies may assume pathogenic significance.

Heredity has long been considered of great significance in the aetiology of respiratory allergic disorders like hay fever and asthma. It has been stressed by some and not without justification that asthma is a symptom-complex resulting from interplay of many forces internal and external. Basic to all asthma is a variable constitutional predisposition. It has been stated by some workers that allergy which is a disordered immunologic adaptive response, disturbs homeostasis and produces disease. The same concept can equally be applied on a cellular or molecular level. The presence of abnormal genes might play a dominant part in the predisposition to allergy. As a result of a random survey, Viswanathan[7] has shown that 29·6 per cent of asthmatics gave parental history of asthma, whereas only 10 per cent of normals gave such history. The family history data collected during the survey provided statistical evidence to show that inheritance in asthma is an autosomal recessive.

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[1] *J. Indian M. A.*, 45 : 512, 1965.

[2] WILLIAMS, R.—Transactions World Asthma Conference, 1965, p. 3.

[3] PEARSON, R. S. B.—*Ibid.*, p. 9.

[4] MONGAR, J. L. AND SCHILD, H. O.—*J. Physiol.*, 135 : 301, 1957.

[5] LECOMTE, J.—*J. Allergy*, 24 : 112, 1957.

[6] SERAFINI, U.—Transactions World Asthma Conference, 1965, p. 73.

We have no correct data about the incidence of allergic disorders in this country. There is however a general impression both amongst physicians as well as the lay public that conditions like asthma, allergic rhinitis and eczema are quite common. Recent morbidity survey[8] conducted amongst the Central Government servants and their families in Delhi showed the incidence of asthma among Government servants to be 1·81 per cent. When the incidence of asthma has been worked out according to salary group, it is found that the rate is higher in the higher income groups than in the lower income groups. The survey showed that in the group whose salary was Rs. 1,000 to 1,500, the rate was 31·7 per thousand whereas in the group in the salary scale ranging from Rs. 75 to Rs. 149 the rate was only 10·6 per thousand.

Elsewhere in this issue will be found the results of a pilot survey[9] conducted in and near Patna. The incidence of asthma in the rural and urban areas surveyed has been found to be 2·7 per cent and 1·6 per cent respectively. It is reasonable to assume that the incidence of asthma for the country as a whole is in the neighbourhood of 2 per cent. If other forms of respiratory allergy are also included the incidence is bound to be as high as 10 per cent.

In spite of high incidence of the disease very little attention has been given to the study of the problem in its various aspects. One of the important reasons why the disease has not received its due attention is the general belief among most of the patients that it is incurable. In the majority of cases the disability in between the attacks is very little. There are many palliative drugs which successfully control even the severe attacks. What has, however, been overlooked is that in the course of years the attacks may lead to increasing disability like emphysema. It should also be borne in mind that the disease can have a fatal outcome especially during status asthmaticus. There is also another erroneous belief that the disease is compatible with long life. It is such misconceptions that have led to inadequate attention being paid to the study of problems pertaining to a serious disease like asthma.

Both the physician and the patient are equally interested in the treatment and its outcome. Asthma being multifaceted, a simultaneous multipronged attack should be made to deal with many factors like infection, allergy, psyche, etc., which seem to be responsible for the development and persistence of asthma. Psychic factor is often neglected in the management of asthma. Even if the disease has started as sensitisation to known allergens, sooner or later, other elements like infection and psychological influence begin to operate and thereby produce a vicious circle.

In western countries like U.S.A. allergic diseases like asthma, hay fever, etc., are being treated by allergists by means of specific hyposensitisation. There is a tendency amongst the allergists to overemphasise the allergic factor. They overlook the fact, that other factors are as much responsible for the development of asthma and similar disorders as sensitisation to allergens. At the same time it must be admitted, that the general physicians have little knowledge about allergy and as such ignore the allergic role in the development of asthma. The time has come when physicians should learn more about allergy and use methdos of specific hyposensitisation whenever and wherever it is warranted. One should not, however, be carried away by the allergists' claim of cure of asthma by specific hyposensitisation. Unfortunately, many patients are sensitised to several allergens. Only a small percentage of cases of asthma is found to be sensitive to a few specific allergens. They no doubt respond to hyposensitisation. In a certain number of cases, infection and/or psyche are superimposed. Unless those factors are also tackled in such cases, side by side with hyposensitisation, treatment will not be successful. A large number of cases mainly due to neglect of treatment in the early stages becomes chronic and intractable. Continuous steroid therapy may have to be resorted to. Attempt to understand the problem of asthma has been totally neglected. The disease can disable. The disease can also kill. Its neglect is inexcusable. It is necessary to rouse the consciousness of the public and the conscience of the physician for promoting research on this important problem of public health.

R. VISWANATHAN

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[7] VISWANATHAN, R.—Respiratory Allergy, 1964, Asia Publishing House, p. 23.

[8] Morbidity Survey of Contributory Health Service Beneficiaries, I.C.M.R. Report, 1961.

[9] VISWANATHAN, R., MODY, R. K., PRASAD, S. S. AND SINHA, S. P.—*J. Indian M. A.*, 45 : 480, 1965.

CURRENT MEDICAL LITERATURE

Chymotrypsin in the Treatment of Peptic Ulcer

AL-SAFFAR, G. I. (*J. Fac. Med. Baghdad*, **7** : 57, 1965) from Department of Medicine, College of Medicine, University of Baghdad, Baghdad, Iraq, reports that chymotrypsin therapy, together with routine dietary and antacid management, resulted in complete cure of over half and improvement in almost a third of 55 patients who had received little benefit from the routine treatment alone. Intramuscular injection of chymotrypsin is recommended for treatment of resistant patients to reduce inflammation and to promote healing, in conjunction with their routine therapy. It is hoped that larger series of observations will more accurately define the place of chymotrypsin in peptic ulcer therapy.

Circulatory Effects of Intravenous Phentolamine in Man

TAYLOR, S. H., SUTHERLAND, G. R., MACKENZIE, G. J., STAUNTON, H. P. AND DONALD, K. W. (*Circulation*, **31** : 741, 1965) from the Department of Medicine, The Royal Infirmary, Edinburgh, Scotland, made circulatory observations on six normal subjects and six hypertensive patients before and after the acute intravenous injection of 5 mg. of phentolamine. The drug caused a prompt reduction in systemic vascular resistance which resulted in a rapid fall in systemic blood pressure in spite of an increase in heart rate and cardiac output.

Evidence is presented that the predominant vascular activity of the drug is to cause a direct relaxation of vascular smooth muscle, an effect far more potent than its antagonism of circulating catecholamines or its very much weaker sympathetic-blocking action. This direct depressor effect on vascular smooth muscle unaccompanied by any but slight sympathetic blocking activities endows the drug with theoretically ideal antihypertensive properties.

Phentolamine caused a transient but significant reduction in oxygen uptake in the majority of individuals. It is suggested that this may be due to a direct inhibition of cellular oxidative mechanisms.

An appraisal of the circulatory activities of the drug with particular regard to its use as a diagnostic test for phaeochromocytoma leads to serious doubts, not only with regard to the precision with which the results of such tests can be interpreted, but also to the validity of the use of the drug as a reliable screening test for excessive circulating catecholamines.

Management of Diabetes Mellitus with a New More Active, Oral Hypoglycaemic Agent (Acetohexamide)

AYAD, H. (*J. Egypt. Med. Ass.*, **47** : 399, 1964) from General Government Hospital and Coptic Hospital, Cairo, used acetohexamide, a new oral hypoglycaemic agent, in the control of the diabetic state in 50 patients with the maturity onset type disease. Used singly in a dose of 1 to 1·5 g. taken once daily in the morning, it could control adequately the disease in 82 per cent of cases. When combined with 25 to 100 mg. of phenformin daily, half of those patients who did not respond initially to the drug ('primary failure cases') were adequately controlled. The maintenance dose varied from 1 to 2 tablets daily (0·5 to 1·00 g.).

The response of a diabetic to the 'intravenous tolbutamide test' enables one to predict the outcome of therapy with acetohexamide.

No major or minor toxic side-effects were noticed, and detailed hematologic and liver function tests, showed no abnormal changes.

Acetohexamide is an adequate hypoglycaemic agent which equals in activity and duration of effect chlorpropamide. Unlike chlorpropamide it does not produce cholestatic jaundice. It is thus a safe hypoglycaemic agent which could be used in the long term management of diabetes mellitus.

Some Aspects of Haemoglobin E and its Genetic Interaction with Thalassaemia

CHATTERJEA, J. B. (*Indian J. Med. Res.*, **53** : 377, 1965) from Department of Haematology, School of Tropical Medicine, Calcutta, makes the following observation :

1. Haemoglobin E was first discovered in 1954. The first patient who showed this abnormal haemoglobin was of Guatemalan origin with Spanish and Hindu ancestry. In the same year, Hb.E was reported from Thailand and in the following year from Bengal. In Hb.E, alpha polypeptide chain is normal. The beta chain is abnormal due to the replacement of the normal glutamyl residue in the 26th fragment by a lysyl residue. In electrophoretic field at pH 8·6, it moves slower than Hb.A and Hb.S but faster than Hb.C. Its solubility is higher than Hb.A. Its alkali-denaturation property and nature of tryptophan band in ultraviolet spectrum are similar to those of Hb.A. It does not have any immunological specificity. Electronmicrographs obtained with the help of negative staining technique employing phosphotungstic acid reveal the characteristic shape and substructure of the Hb.E molecule. While some of the molecules have an ellipsoidal appearance, in many instances the shape is asymmetrical and pointed towards one end. The average of the maximum and minimum dimensions of stained molecules approximate 78A°×62A°. The sedimentation constant studied in ultracentrifuge is 4·56, a value similar to that of Hb.A.

Discovery of haemoglobin E in Bengalees has solved the problems centering round the diagnosis of hereditary haemolytic anaemias and their variation in clinical features, haematological manifestations and genetic background. The incidence of Hb.E is 3·9 per cent in general Bengalee population. Heterozygote and homozygote subjects of Hb.E have been investigated and their clinical, haematological and relevant biochemical status delineated.

2. In Bengalees, incidence of thalassaemia has been found to be 3·7 per cent. Genetic interaction of thalassaemia and Hb.E gives rise to the double heterozygote condition of Hb.E-thalassaemia disease which is the commonest form of haemoglobinopathic disorder seen in Bengal. Comprehensive investigations and follow-up studies in a large series of cases of Hb.E-thalassaemia disease have provided interesting data on the nature of erythropoiesis, stability of red cells, status of erythrocytic reduced glutathione and related enzyme systems, results

of splenectomy and interrelationship with certain environmental factors.

3. In the present state of our knowledge, therapeutic prospects of severe cases of Hb.E-thalassaemia are unsatisfactory. It is expected that in some cases, the genetic handicap is further worsened by an environmental stressor which may timely be withdrawn to produce significant amelioration. In view of our limited ability to help the severe cases, it is desirable to devise ways and means of evolving adequate preventive measures. In the present state of our knowledge this may be achieved through premarital examination of blood. This examination is imperative with reference to apparently normal subjects of a family in which one or more cases of haemoglobinopathic disorder have occurred.

Cardiac Surgery and Pregnancy

UELAND, K. (*Amer. J. Obstet. Gynaec.*, **92** : 148, 1965) from the Heart Research Laboratory, University of Oregon Medical School, writes :

Approximately one pregnant patient in 80 has heart disease. Improved medical and surgical management has reduced the maternal mortality rates from toxaemia, haemorrhage and infection. Although maternal deaths from heart disease have declined, this group now comprises one of the major causes of maternal mortality. Most authorities feel that careful and strict medical management is preferred for the pregnant cardiac patient, surgery being reserved for the few patients with mitral stenosis who show progressive disability early in pregnancy and for those with refractory failure or severe haemoptysis. Eastman, in agreeing with Gilchrist, writes, "The most important factor in the reduction of maternal mortality in the past 30 years is the employment of prolonged bed rest in the hospital.

Indeed, by and large, the best management of desperate heart disease in pregnancy is not therapeutic abortion or valvotomy but hospitalisation throughout pregnancy, usually with complete bed rest. But valvotomy in pregnancy does have a place, it seems to the author, even if a small place. This is in the patient who decompensates early in pregnancy and in whom bed rest and the other usual measures do not completely restore compensation within a fortnight or so. The question is not whether cardiac surgery can or cannot be performed during pregnancy but rather when it is indicated in the over-all management of the pregnant patient with heart disease. With increasing experience and perfection of surgical and technical skill heart surgery will become an increasingly important adjunct to medical management.

Future statistics will indicate the safest and best time for cardiac surgery. At present long-term benefits from heart surgery during pregnancy have not been clarified. When the decision for surgery is made the best operation for each patient must be performed. Reoperation is difficult and dangerous and the results are generally unsatisfactory. All these principles should be considered and carefully weighed as one assumes the responsibility for the care of the pregnant patient with heart disease and before any active surgical intervention is undertaken.

Malignant Hepatoma in a Child : Survival following Right Hepatectomy, Right Pneumonectomy, and Resection of Diaphragmatic and Parietal Recurrence

BRADHAM, R. R., PAUL, J. R., THROWER, W. B. AND MCIVER, F. A. (*Surgery*, **57** : 767, 1965) from the Departments of Surgery, Pediatrics, and Pathology of the Medical College of South Carolina, report an unusual case of malignant hepatoma in a 21-month-old child. The patient has survived for 4 years following resection of the primary tumour by right hepatic lobectomy, and for more than 3 years following right pneumonectomy and resection of an area of chest wall for recurrences. Presently no evidence of disease is detectable. A detailed account of the history, physical findings, laboratory data, and course of illness is given. The pathology of the tumour is described and illustrated. An unusual haemolytic crisis associated with a hereditary abnormal haemoglobin glutathion sulphydril and occurring in the posthepatectomy period is discussed. The experience and observation of others interested in this childhood neoplasm, which has such a very poor prognosis, is cited. The rarity of a cure for this malignancy makes this case meaningful. Early diagnosis and hepatic lobectomy will probably result in a higher incidence of cure in the future. This is the only effective method of therapy presently available.

A Study of Gonococcal Infections among Infants and Children

BRANCH, G. AND PAXTON, R. (*Pub. Hlth. Rep.*, **80** : 347, 1965) from the Los Angeles County Health Department, write :

In a study of 180 children under 15 years of age with gonococcal infections, conjunctivitis was observed in all the infants under 1 year of age and infections of the genitals in all the children aged from 1 to 14 years. Complications involving the conjunctiva, joints, urethra, rectum, or tubes occurred in 6 per cent of all the children.

Gonococcal infections in infants under 28 days of age were associated with infections in the birth canal of the mothers. In infants under 1 year old, the infections were attributed to poor personal hygiene practices of the parents. These practices as well as molestation by relatives also accounted for most of the infections in the children under 9 years of age.

Among the children aged 10-14 years, the infections were associated with unsatisfactory parent-child relationships, overcrowed homes, and sexual activity outside the home. Ninety per cent of the infections in this age group resulted from boyfriend-girlfriend relationships or casual acquaintances.

The incidence of gonorrhoea among children aged 10-14 years has been increasing constantly in Los Angeles since 1960, and this situation is occurring in many other cities. In order to stem the rates of infection among young adults, the infected 10 to 14-year-old children must be helped to understand their condition. The public health liaison nurse can make an effective contribution by providing sex education, which includes an explanation of the mechanism by which they became infected, by obtaining a history of contacts and associates, and by arranging for follow-up.

CURRENT TOPIC

THE WORLD ASTHMA CONFERENCE

The Chest and Heart Association's World Asthma Conference held in Eastbourne, Sussex, on March 23 to 26, 1965, was a tremendous success.

Her Royal Highness Princess Marina, President of the Association, in her opening speech reminded the seven hundred delegates that it was the sixth CHA Conference she had opened since she took her husband's place as President in 1943. Princess Marina hoped it would play an important part in benefiting asthma sufferers everywhere.

The Sir Robert Philip Medal, awarded at CHA Conferences every three years for outstanding work in the fight against tuberculosis in the Commonwealth, was then presented to Sister Mary Aquinas, the first woman to receive it.

Dr. Norman Lloyd Rusby, Vice-Chairman of the Association, spoke about Sister M. Aquinas' work and career. A Missionary Sister of the Congregation of St. Columban, she studied medicine at University College, Dublin, following her religious profession. She then did postgraduate medical work in London and Cardiff, going to Hong Kong as Medical Superintendent of Ruttonjee Sanatorium in 1949. The sanatorium with 230 beds occupied mainly by tuberculous Chinese patients, in spite of poverty and malnutrition almost inconceivable in the West, has all the resources of modern treatment. Sister Mary Aquinas, in addition to clinical work and lectures, has found time for original research and has taken part in trials of chemotherapeutic substances.

Lord Taylor, Under Secretary of State for the Colonies, speaking on behalf of Mr. Anthony Greenwood, read a letter expressing the Secretary of State's regret at not being able to attend. He spoke also of the great work done by Sister M. Aquinas in Hong Kong, and of the urgent need for doctors and nurses to work in the under-developed countries.

Following Lord Taylor's speech the first session was opened by Dr. John Fry with a talk on the natural history of asthma as seen in general practice. The general practitioner has a unique opportunity of assessing the incidence of asthma, the effect of environment and the progress of the disease. Dr. Fry analysed 110 asthmatic patients seen and followed up for fifteen years. They represented an annual prevalence of 12 per 1,000 of the population of the practice. He said that they came chiefly from the more well-to-do classes. In most of them the disease began in childhood. One third of the males and one half of the females had emotional difficulties; one third of the males and one fifth of the females had allergic states of other kinds; one fifth of all had a family history of asthma or hay fever. Severe disability was present in only 5 per cent after fifteen years. He thought there was therefore an important tendency towards natural and spontaneous improvement.

Dr. Michael Hume, from the King Edward VII Hospital, Midhurst, defined intrinsic asthma, which usually showed itself in adult life, infrequently at first, but with attacks becoming increasingly frequent. There was usually no allergic reaction to extrinsic substances. A family history of asthma, hay fever or allergic rhinitis was common. Respiratory infection was the commonest aetiological factor. Changes in the weather and in atmospheric condition could bring on attacks.

During the second session on respiratory function in asthma, Dr. Ronald S. McNiell analysed the effect of exercise in asthmatic subjects. Professor Bryan Gandevia, of Sydney, Australia, pointed out that there were many athmatic cases known to respond subjectively to treatment, without showing much or any physiological improvement. Reversibility in asthma could not yet be considered, as it logically should be, in terms of the mechanisms causing bronchoconstriction. Less was known of the factors involved in spontaneous reversibility than of those concerned with the development of bronchoconstriction. On the other hand, we were steadily gaining a better quantitive understanding of the response to bronchodilator agents, so that therapy might be planned on a more rational basis than was formerly possible. The realisation that relaxation was able to produce significant clinical reversibility and improved ventilatory efficiency offered not only a valuable therapeutic weapon but also, its linkage of psyche and soma, a more fundamental understanding of asthma. The reversibility induced by steroids, at times more dramatic, contributed less to understanding. He challenged doctors who believed in dogmatic classification, emphasising that there can be no absolute criterion, because knowledge of the subject is totally inadequate. The session, with Professor John Crofton, Department of Respiratory Diseases and Tuberculosis, Edinburgh, in the chair, was lively and stimulating, and extra time was allowed for the many questions.

For the third session on the fundamental approach to the mechanisms of asthma, Dr. Jack Pepys was in the chair. Dr. J. L. Mongar, from University College Hospital, London, described research undertaken on anaphylactic reactions and the mechanism of the release of histamine in those reactions. Anaphylactic reactions could be inhibited by substances which blocked sulphydryl groups, by thiol components, by protein denaturants and by anaerobic conditions. There was eivdence of an enzymatic reaction, but at present the anaphylactic enzyme system could not be equated with any known enzyme system. Work was continuing.

Dr. Rosa Augustin spoke on reagins, their structural and biological differentiation from other antibodies and their *in vitro* estimation.

Dr. Walter E. Brocklehurst of the University of Edinburgh spoke on Slow-Reacting Substance A and Bradykinin, making a critical survey of the present position concerning knowledge of SRS-A and the contribution it makes to the symptoms of asthma. If SRS-A had proved to be one of the known active substances of the body, no doubt some therapeutic advance would have resulted by now. However, all the evidence showed that SRS-A was a 'new' substance and that it was extremely potent. The amount of negative evidence (i.e., showing what SRS-A was *not*) was considerable, but there was no lead, as yet, to what SRS-A *was*. Studies had shown that SRS-A must be a small molecule. He hoped that these studies would soon lead to the preparation of enough 'pure' material to permit chemical identification. This was the crest of the hill. Once the chemistry of SRS-A was known, the precursor and the enzymic mechanisms of formation should be easy to find, and real possibilities of advance in medical treatment should be apparent.

Professor R. G. White discussed the role of mycobacterial components in altering the immunological responses.

In the meantime other delegates were attending meetings on the more emotional aspects of the condition. In a group discussion under the chairmanship of Dr. David Lawson, tension and fear in relation to asthma were discussed by Dr. Lionel E. Houghton, who described bronchial asthma as a pattern of behaviour rather than a disease, in which symptoms were due to an exaggerated response to environmental stimuli. Delegates questioned the wisdom of hypnosis therapy, suggesting there was a danger of merely reducing symptoms, with a possible later transference.

This theme was developed in the following session, psychological factors in asthma, in which the divergence between specialists in the allergic and in the psychological aspects of asthma became noticeable. The chairman of this session was Dr. Linford Rees, and papers were read by Professor J. A. Groen of the Hebrew University, Jerusalem and by Professor Jan Bastians of the State University, Leiden, The Netherlands. Dr. G. P. Maher-Loughnan described the use of hypnosis and autohypnosis in treatment in cases where the asthma was fairly severe, the patient had not had steroid treatment, and was mentally sound. At first the physician induced hypnosis and then by a post-hypnotic suggestion, the patient was given the ability to enter the hypnotic state of his own volition. The autohypnotic state lasted fifteen minutes each day and must be induced daily. Results had been encouraging both subjectively and objectively on tests of pulmonary function. Autohypnosis perpetuated relief and diminished patient-doctor dependency.

Miss Theodora Alcock, Tavistock Institute, London, investigated the personality features of 25 asthmatic children, comparing them with three control groups. On this basis the asthmatic personality appeared to be marked by depression (in contrast to a cheerful facade), emotional sensitivity in human relationships, combined with excessive control, disturbed reactions to effective stimuli, persecutory ideas and social compliance. There was a state of intolerable emotional tension without appropriate outlet.

Dr. Albert Mason, King's College Hospital, London, sounded a warning note on treatment by hypnosis. He considered that some patients so treated showed only subjective improvement, without corresponding relief in the organic component of the disease.

The session on Special Problems of Asthma in children, with Dr. N. Lloyd Rusby in the chair, was opened by Dr. C. Eric Stroud, King's College Hospital, London, who discussed the diagnosis in infants suffering from acute bronchiolitis, in which the clinical condition was very much like that of asthma.

Dr. J. Morrison Smith, from the Birmingham Chest Clinic, drew attention to the fact that severe bronchospasm, unrelieved by anti-spasmodics, should not be allowed to continue for days, even if the child was reasonably free of distress at rest. Steroids should be used in effective doses in order to prevent any possibility of an unexpected fatal outcome. Most children responded to small doses of steroids, but these should be used as adjuncts to anti-spasmodics, never as substitutes. He stressed that for children education was most important. It might be a question of enabling them to undertake comfortable work in which a full life could be expected. Special residential schools could be of wonderful benefit.

Dr. Margaret Scott Stevenson's paper on the educational services available to the asthmatic child produced a number of questions. Some delegates thought it preferable for asthmatic children to attend ordinary rather than special schools. An American delegate commented particularly on the different approach of the British and Americans. In England the child was educated, and incidentally was asthmatic. In America he was an asthmatic sent for treatment, and incidentally was educated.

A sidelight on the treatment of asthmatic children was given by Dr. Hans Meyer who described treatment given at high altitude in Switzerland. Asked by one delegate whether separation from parents during prolonged treatment had any ill effects on the child, he replied that this had occasionally been known in Swiss children, but very rarely in children from Britain, which brought a gust of wry laughter from the hall.

In the session on allergy and infection, the chairman, Dr. A. W. Frankland, pointed out that asthma was due to many causes. The asthmatic subject had been likened to a gun that was loaded. We understood little why the gun was loaded and could not always find out what triggered off the attack. The allergic trigger when present was the easiest to treat successfully. Asthma due to one cause only was uncommon, yet allergic asthma by itself did occur and could commonly be precipitated by house dust, animal scurf, fungal spores or pollens. Doctors could not easily prevent infection, psychiatrists could not easily help their patients, but we could do a lot for our allergic patients. This field in asthma had made great advances in the last few years.

Dr. Marie Britt Rhyne of the Johns Hopkins Hospital, Baltimore, U.S.A., spoke on allergic factors in asthmatic children, and stated that allergy could be defined as an antigen—antibody reaction causing tissue damage. It was generally held that in asthma the type of allergic reaction was the local anaphylactic type, which was initiated by allergens reacting with tissue cells sensitised by antibody leading to the release of pharmacologically active substances such as histamine and Slow Reactive Substance A. Consideration of measures aimed at prevention of antibody production or prevention of reaction of the antigen-antibody complex should be entertained. As we became more aware of the nature of the susceptible population to develop antibodies, and its relationship to the total population susceptible to develop symptoms of asthma then a clearer picture of the nature and importance of allergic factors in asthmatic children should be determinable.

During the discussion, Dr. Ian Morrison of Brisbane, Australia, pointed out that under the Colombo plan a large population of students was coming to all universities in Australia. These students had not suffered from any particular allergic disease in their own country, but after a short time in Australia developed hay fever and/or asthma. The students were Chinese, Malays, Indians and Thais. Dr. Morrison thought this was not due to economic factors but to local factors where the students encountered many strong sensitisers giving rise to allergic asthma. Dr. Frankland brought out that in this country many immigrants to Great Britain, particularly those from the West Indies, developed hay fever and asthma for the first time after three years here. Their children born in this country had a higher incidence of eczema than British children, whereas it was very rare in the West Indies. Dr. Mahdi from the Sudan said that in his country, and he thought in other developing countries, they were seeing many of the diseases of civilisation which they used not to have, including asthma.

Asthma occurring regularly at the same time each year should always be regarded as of possible allergic origin. The seasonal nature of the complaint was sometimes completely missed, either due to lack of observation on the part of the patient or lack of detailed history-taking on the part of the doctor, Dr. Douglas Blair Macaulay said. He discussed allergenic contaminants of the air, and pointed out also that occupation played some part in producing a seasonal asthma. Market gardeners could be affected by the moulds occurring on tomatoes, cucumbers and chrysanthemums, and farmers by potato blight or by the rusts and smuts which appeared just before the grain was cut or during threshing. As was the case with all allergic diseases, avoidance where possible of the offending allergen was the best treatment. This might not be possible in many cases and hyposensitisation might then need to be considered.

Sir Hugh Beaver, KBE, chaired the welfare and rehabilitation services session, in which the speakers included Dr. G. M. O'Donnell, Medical Officer of Health for Worcester, who pointed out the importance of selecting the right school for asthmatic children. A child overprotected at home and school might develop a difficult personality. On leaving school he was subject to the stresses of home and the need to earn a living, which might provoke fresh asthmatic attacks. He mentioned various agencies which could help, and emphasised the fact that much sound advice was available to parents.

Miss Pamela H. Lewis, of the Department of Social Work, London Hospital, described the place of the social worker in uncovering home conditions, such as damp and moulds, relevant to asthma. While the psychological environment of children was often faulty, she stressed the fact that their removal from such an environment might not be the wise course.

Miss Jacqueline M. Knight, Social Worker to the British Red Cross Society, spoke of high altitude treatment at Davos, Switzerland, where selected British patients, children and audlts, might be sent. The importance of understanding, co-ordination of effort, and after-care was urged. Many children had led sheltered lives and did not know how to live with their asthma.

Miss Grace D. Rattenburg, of the Invalid Children's Aid Association, London, spoke of the schools set up by the Association, stating that their aim was to remove selected children temporarily from the stresses to which they had been exposed, and to enable them to regain self-confidence.

Mr. J. Elliott, an asthmatic patient who is an assistant lecturer in Government and Economics, Newcastle-upon-Tyne, described his own experience. Because of asthma, his education had been defective, but through attending evening classes he eventually reached University and took a B.A. Hons. degree. He was highly critical of the medical profession, the educationists and the trade unions. He thought there was too little preventive medicine, that doctors were not forthcoming enough about treatment, and that too little attention was paid to environment and diet.

Dr. H. M. Carryer of the Mayo Clinic, Rochester, USA, in the session on the general management of the asthmatic patient, chaired by Dr. A. W. Frankland, described the treatment of status asthmaticus. The first drug should be a bronchodilator such as epinephrine, in sufficient doses given frequently enough. The patient was often dehydrated, and intravenous fluids were needed. Expectorants helped to thin the bronchial secretion. Moderate sedation was called for, but not with opiates. Steroids should be used only when indications were compelling. Oxygen might be needed. Antibiotics should be used for bronchitis due to infections. He stressed that the whole patient—his other diseases, his emotional problems and the ultimate effects of treatment- should be observed and treated.

Dr. I. W. B. Grant, of Edinburgh, discussed the treatment of chronic asthma with corticosteroids, and Professor John Briggs, from the University of Minnesota Medical School, USA, gave a paper on the heart condition in asthma.

In the group discussion on the parental role in asthma, chaired by Dr. Harley Williams, Dr. Monica McAllen of University College Hospital, London, pointed out that many allergists had seen children with a predominantly allergic condition, which had been wrongly ascribed to emotion engendered by wrong attitudes in the parents, and which had responded to desensitisation. The components—allergy, infection and emotion—needed to be recognised and evaluated. She emphasised the value of sympathetic explanation to parents, who should be advised to approve their children for what they were, not for what they could do. Children should be encouraged to develop personal independence. During the discussion Dr. W. J. Wigfield spoke as a school doctor. He disagreed with a speaker who thought that parents of children with repeated attacks of asthma were unaware that they were mishandling their children. Dr. Wigfield thought that the majority did realise to some extent and they felt they were failures as parents. All parents made mistakes in handling their children, but on the whole were able to learn from their mistakes. However, if the child had asthma whenever the parent made a mistake, he could not learn how to handle the child and passed on his own feeling of insecurity to the child. He thought the experience of a speaker who found great improvement in the parental attitudes after the asthma attacks ceased bore out this opinion.

In his own group discussion, the asthmatic child at school, Dr. Wigfield said that life at school for an asthmatic could be more of a burden than was generally realised, and this might give rise to another situation—the use of asthma as an escape. The result might be a spoilt child. By no means all asthmatics developed this behaviour pattern, but there was always a risk of it. The school doctor had a contribution to make in three main spheres: discovering asthmatics, ensuring that they were receiving proper treatment and advising the school about their physical activity. He said the function of education was to fit children to take a constructive place in the world. Asthmatic children wanted to do this, and to be on equal terms with their friends. They could best be helped, not by offering special assistance all along the line, but by helping them to help themselves. Mr. B. G. Savage, headmaster of Warnham Court School, took the chair during this meeting.

Dr. W. A. Murray was in the Chair for the group discussion on training, employment and welfare problems in which Dr. Robert Murray, Medical Adviser to the Trades Union Congress, commented on the increasing number of industrial processes which appeared to carry risk to workers of "occupational asthma." Feathers and wood, particularly teak and red cedar, had proved dangerous in this respect. In the textile industry size prepared from tamarind seeds had apparently caused a severe reversible asthmatic upset in many workers. He discussed an interesting finding of asthmatic symptoms with nausea in workers exposed to isocyanates in the manufacture of foam plastics. During the discussion one of the points raised was the need for better team-work between general practitioners, school medical officers and factory doctors. Would it not be possible for school records to go automatically into industry with school-leavers delegates enquired?

Dr. J. A. Crockett, of Glasgow, discussed the effects of altitude, climate and air pollution in the aetiology of asthma in another group discussion. High altitude was in general favourable in reducing attacks. There was a strong relationship between asthma and certain phases of weather, the frequency increasing rapidly after a sudden increase in general turbulence with influx of cold air masses. High altitude was probably a factor, as also was the level of suplhur dioxide in the air. He thought that these three factors might influence air ionisation, and variation in this might be important. Dr. I. C. Morrison of Brisbane, Australia, said that both he and the Queensland Institute of Medical Research had found a correlation between southern maritime air and a marked increase of asthma. There appeared also to be a correlation with dew point, as this is a factor of humidity and temperature drop. The first big drop in temperature came in March when asthma began to increase, reaching a peak in late April. Mr. A. C. A. Colton was in the chair.

A number of visits and tours were arranged to special schools, including Pilgrims School, Seaford, and Warnham Court Open Air School, near Horsham; to Benenden Chest Hospital, Kent, and King Edward VII Hospital, Midhurst, Sussex. Two visits arranged for the benefit especially of overseas doctors were the Bencard Allergy Unit Research Laboratories, and the Chest Disease Department of Hammersmith Post-graduate Medical School, where Dr. C. M. Fletcher and Dr. E. J. Moran Campbell gave a lecture and demonstration.

Films were shown each day of the Conference, including Allergy (16 mm. colour); British Children Take the Waters (16 mm.—loaned by International Help for Children); Physiotherapy for Asthmatic Children (16 mm. colour). One of the finest films was a German documentary on the physiology of pulmonary function and the methods used in its study (16 mm. colour—loaned by Boehringer Ingelheim Ltd.); Pulmonary function (16 mm. colour) dealt with the three main aspects of respiration, and the final feature was Recurrent Bronchitis and Intrinsic Asthma (16 mm. colour).

Nearly every session of the Conference provided valuable opportunities for experts to agree and disagree, to question and qualify. End of session questions tended to indicate the totally different approach of, for instance, specialists in the field of allergy and those primarily interested in psychological medicine. Generous time was allowed for discussion, yet so stimulating were the meetings there never seemed enough for real expansion on the questions asked, though most delegates seemed to remedy this between sessions. Would the meetings have perhaps been even more valuable if the apparently opposing sides had been able to find the time to participate more actively in sessions outside their own specialities? There can be no doubt that prolonged discussion between exponents of these differing schools of thought could be extremely fruitful.

NOTES AND NEWS

Hamdard Foundation Award

Prof. R. B. Arora, Professor of Pharmacology of the All-India Institute of Medical Sciences, New Delhi, has been given the Hamdard National Foundation Award of Rs. 10,000.

The award has been given for his outstanding work on some indigenous drugs useful in cardiovascular diseases.

This is the first award given by the Foundation which has been established for the promotion of research in indigenous systems of medicine.

2-Man Team to Probe into Adulteration

Dr. Sushila Nayar, Union Health Minister, said in the Lok Sabha that a two-man committee had been appointed to visit various States to collect necessary information on the effectiveness of the machinery to implement the anti-adulteration law and laboratory facilities.

The information collected would be placed before the Central Committee of Ministers for their consideration.

Friend Virus Attacks Platelets

An experimental leukaemia virus has been found to ause blood platelet and megakaryocyte disruption. The liscovery may throw light on the problem of haemorrhge in human leukaemia.

Two investigators at Hahnemann Medical College, hiladelphia, Dr. Isadore Brodsky and Dr. Lewis H. ennis, have found that 48 hours after infecting mice vith Friend virus, blood platelet levels had decreased by quarter.

Some of the animals died from splenic rupture, suffering major interference with the reticulo-endothelial system in 10 to 30 days after infection.

Most of the mice, however, continued to live for 50 to 80 days after infection and died of leukaemia.

Friend virus was discovered nearly ten years ago by Dr. Charlotte Friend working at the Sloan-Kettering Institute, New York. Infection results in death from leukaemia in some 80 per cent of mice within about three months.

Like virtually all the known viruses associated with experimental malignancy, the Friend agent is an RNA virus.

Summarising this latest work, Dr. Brodsky believes that when Friend virus infects a mouse this is what happens :

1. The virus invades the megakaryocytes taking the place of normal cell RNA in the classical picture of viral infection.
2. The RNA in the infected cells now produces virus instead of platelets.
3. The spleen enlarges as the cells in the endoplasmic reticulum become attacked by the virus.
4. Finally with the platelet complement depleted and the vessel wall competency challenged, the animal bleeds to death from ruptured and unrepaired small vessels.—*Medical News.*

Acid Test

Countless coronary-conscious American males dutifully avoid fried foods, shun butter and pour skimmed milk into their coffee in the hope of preventing heart attacks. But in Norway, some 7,000 men in their 50s are currently testing a much simpler regimen—a daily tablespoon of tasteless linseed oil.

This vast experiment is based on research by Dr. Paul A. Owren of Oslo's University Hospital and described in a recent issue of the *Annals of Internal Medicine,* Journal of the American College of Physicians. The new approach is intended to forestall coronary thrombosis, the blood clot that finally blocks the vital coronary artery, causing more than half of heart-attack fatalities.

According to Owren, a 60-year-old expert in the mechanisms of blood clotting, the stage is set for coronary thrombosis when platelets tend to attach themselves to the artery wall and form a clump. Later, the potentially fatal blood clot forms over these platelets, blocking the artery. In blood tests, Owren found that the platelets of persons known to have coronary disease had an abnormal tendency to clump; thus if some way can be found to correct the abnormality, thrombosis might be prevented.

The growing suspicion among heart disease experts, of course, is that the types of fats consumed in a person's diet affect the chances of heart attack. So Owren decided to see what effect fats had specifically on platelet clumping. He found that linseed and soybean oils, which are rich in linolenic acid, reduced the platelet clumping tendency to normal.

What's more, Owren uncovered encouraging statistical evidence linking linolenic acid in the diet to a reduction in heart-attack risk among Norwegian men. In the valley of Gudbrandsdal, Owren noted the death rate from heart attacks was only a third of the toll in Oslo. The typical diet among North Gudbrandsdal farmers, he also found, was unusually high in linolenic acid because the men ate considerable amounts of whole-flour products. And unlike the typical Oslo men, the farmers consumed little margarine, which in Norway, is made from whale oil, a fat extremely low in linolenic acid.

To help put Owren's theory to a test, under a study directed by the Norwegian Council of Industrial Medicine, some 14,000 workers pick up a bottle of oil each month from plant doctors. Since the study is "controlled," half the men get linseed oil, the rest, corn oil. By next March, comparison of heart-attack rates may tell whether Owren has found a way to curb coronaries. —*Newsweek.*

Drug Hazards

The 18th World Health Assembly meeting at Geneva Assembly discussed various problems relating to the protection of individual and public health against the hazards arising from the biological effects of drugs. The importance of the systematic collection, evaluation and dissemination of information on adverse drug reactions was stressed, and Member States were invited to develop national monitoring systems for such reactions as soon as possible with a view to taking part in an international system under the aegis of WHO. The Director-General was asked to continue studying the requirements of an international programme for the collection analysis, and distribution of information in this field. The U.S. Government has offered to provide WHO with facilities for the processing of information on adverse drug reactions by means of a recently developed computer system.

The Single Convention on Narcotic Drugs, 1961, came into force on 13 December, 1964. The functions of WHO under this Convention include making recommendations on the international control status of certain drugs to the Commission on Narcotic Drugs of the Economic and Social Council. The Assembly considered that it would be advisable to amend the Convention to give WHO the power of decision in this field that it has held under previous treaties. Member States were urged to become parties to the Single Convention in order to ensure the universality of its application.

Speaking in support of a draft resolution on the contral of dependence-producing drugs, Dr. A. Engel, Chief Delegate of Sweden, stated that during the past decade the abuse of certain types of drug not covered by international narcotics control conventions had been increasing to a large extent, particularly among young people. He cited examples from his own country, where control

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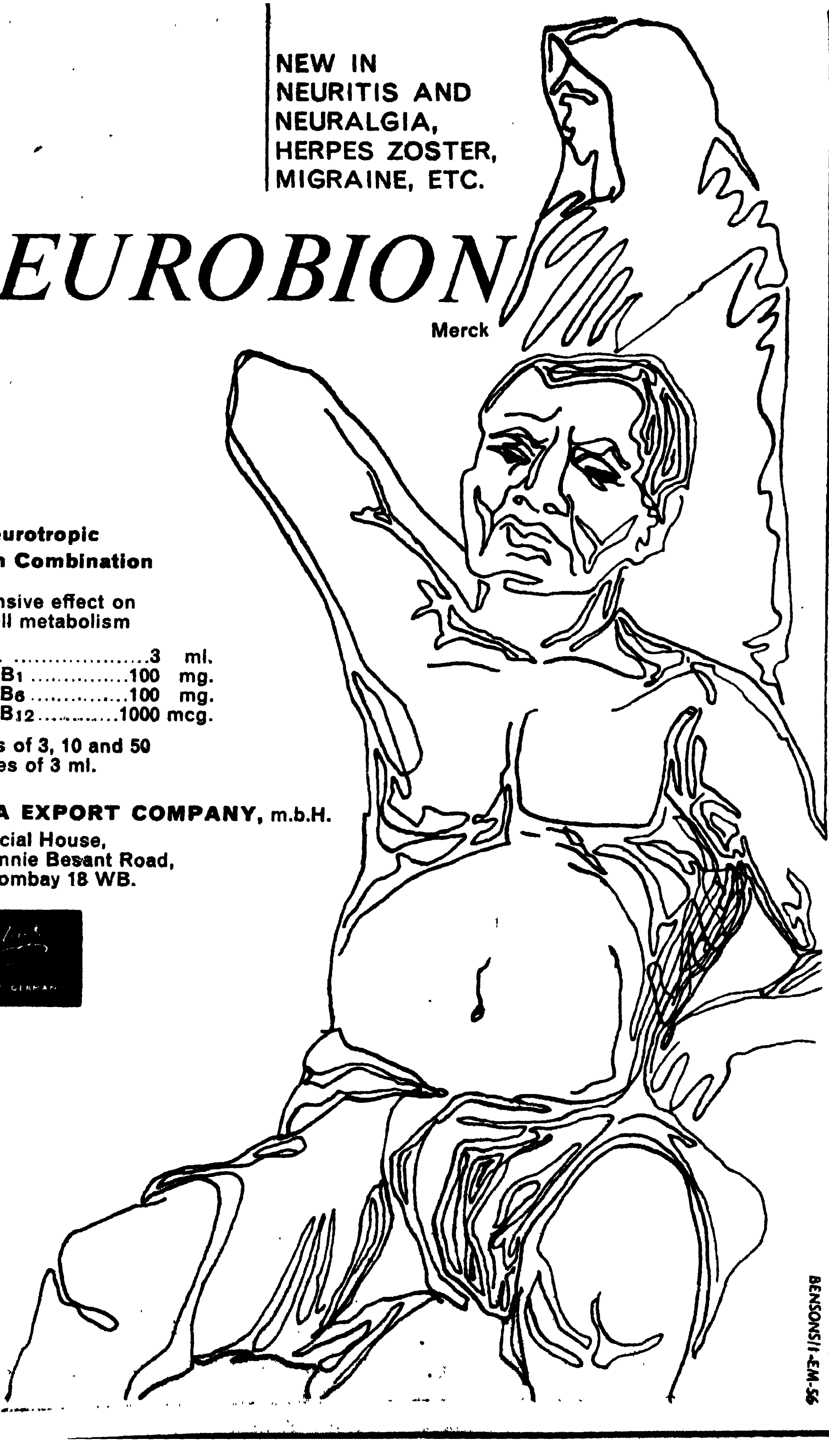

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measures are ineffective because many pharmaceutical preparations requiring prescriptions in Sweden may be obtained freely in other countries. An illicit traffic in many of the dependence-producing drugs has accordingly developed between these countries and Sweden. There is thus a need, Dr. Engel felt, for the immediate adoption and application of international control measures to the amphetamines and barbiturates and to other stimulants and sedatives.

A number of delegates doubted the advisability and feasibility of international measures to control sedatives and stimulants in the same way as narcotic drugs, and the Assembly therefore asked the Director-General to study this aspect of the problem. It was recommended that Member States, which had not already done so, should place widely abused sedatives and stimulants on medical prescription and promote intensive health education on the dangers of their abuse. The promotion of further research into the epidemiology of drug dependence was also recommended.—*WHO Chronicle.*

West Bengal Medical Council

Dr. S. K. Ghosh, Registrar, West Bengal Medical Council states :

The attention of all Registered Medical Practitioners is drawn to Section 16(2) of the Bengal Medical Act, 1914, in obedience to which the names of Registered Medical Practitioners are erased from the Council's Register from time to time for failure on their part to reply to the Council's query regarding their present address and continuance of practice.

Under the recent I.M.C. (Amendment) Act, 1964, as published in the *Gazette of India* dated 17-6-64 practice of Allopathic System of Medicine by any person who is not registered with any State Medical Council is forbidden and the defaulter is liable to punishment as provided in the amended Sec. 15 of the I.M.C. Act, 1956.

All Registered Medical Practitioners of this Council are, therefore, advised in their own interest as well as for the interest of their patients to consult the up-to-date Medical Lists published by this Council (available for public inspection in the office of the Council at 8 Lyons Range, 3rd Floor, Calcutta 1) be satisfied that their names are still borne in the Register of this Council and to take necessary action for restoration of their names if actually erased. It is regretted that letters of enquiry in this connection cannot be attended to due to paucity of staff.

World Congress of Cardiology

The 5th World Congress of Cardiology will be held from October 30 to November 5, 1966, in India for the first time. An Organising Committee has been formed with the following : President—Dr. K. K. Datey (Bombay); Vice-Presidents—Dr. V. V. Shah, Dr. T. H. Tulpule, Dr. S. J. Shah and Dr. I. J. Pinto (Bombay) and Prof. K. S. Mathur (Agra); Secretary General—Dr. S. Padmavati (New Delhi); Joint Secretary—Dr. S. B. Roy (New Delhi); Additional Joint Secretaries—Dr. N. S. Dixit and Dr. P. D. Nigam (New Delhi) and K. B. Bakshi (Calcutta); Treasurers—Col. Amir Chand and Mr. Mohan Singh (New Delhi) and Dr. D. P. Basu (Calcutta).

The office of the Organising Committee is located at 118, Bangla Sahib Marg, New Delhi, and the telegraphic address is CARDIOCON.

The last date for submission of papers to National Societies of Cardiology and submission of application for scientific exhibits to reach New Delhi is 31-1-66.

The last date for receipt in Delhi of abstracts of papers, and summaries of round tables, symposia and lectures, and application for membership is 31-3-66. The last date for receipt of full texts of papers, etc., in New Delhi is 1-7-66.

All members of national societies of cardiology which are affiliated to the International Society of Cardiology are entitled to become members of the Congress and will have the privilege to present papers, participate in scientific discussions, and in all the social and cultural activities scheduled during the Congress. Members of the medical profession who are not members of any national society of cardiology can also attended the Congress on payment of fee. All papers will be submitted through national cardiac societies, except where they do not exist.

There will also be associate members, mainly relatives of Congress members. They will not participate in the scientific sessions of the Congress, but will enjoy the other privileges of Congress members.

The Registration fee for members is U.S. $ 50 or Indian Rupees 238 and that for associate members U.S. $ 25 or Indian Rupees 119. Registration fees for those registering after April 30, 1966 will be higher.

Bulletins of the Congress will be in English, French and Spanish. Simultaneous translations in English and French will be available only during the morning sessions—symposia, round tables, and lectures. For the afternoon sessions when individual papers will be presented, translations, tape-recorded earlier, will be used.

The Opening Ceremony will take place on 30-10-66 and the closing ceremony on 5-11-66. Scientific Sessions will be held from 31-10-66 to 5-11-66.

The subjects for symposia and round tables are as follows : Current status of the Study of Cardiopulmonary Function—Methods of Application. Evaluation of Cardiovascular and Cardiopulmonary Function after Cardiovascular Surgery. Exercise Tests in Evaluation of Cardiovascular Function. Application of Computer System in Cardiovascular Research. Present Status of Prevention of Rheumatic Heart Disease. Precocious Ischaemic Heart Disease. Aetiology and Pathogenesis of Cardiomyopathies. Current Status of Cardiovascular Surgery. Thermal Stress and the Cardiovascular System. Preventive Aspects of Heart Disease.

An exhibition of scientific material—graphs, tables, legends, photographs, slides, etc., and a commercial exhibition of manufactured products—pharmaceuticals, chemicals, devices, instruments, etc., will be held in Vigyan Bhavan, the premises where the Congress will be held. Social and cultural programmes for the delegates and the ladies will also be arranged on different dates.

SITA World Travels (I) Pvt. Ltd., Imperial Hotel, Janpath, New Delhi, India and their branches have been appointed as official travel agents of the Congress.

REVIEW

Clinical Examination—By Thomas N. Stern, M.D., 1964, Year Book Medical Publishers, Inc., Chicago; 15 cm. ×22·5 cm., pp. 381; $8·50 net.

This new book on physical diagnosis describes the standard methods of bedside examination and discusses the findings in many of the common clinical conditions. It contains much useful knowledge which is presented in a discursive manner. The book will prove useful to students and practising physicians in developing their clinical diagnostic skill. It is attractively set out and profusely illustrated. The book contains many unnecessary eponyms.

J. Dhar

OBITUARIES

Dr. D. Sitaramayya

Dr. Duggirala Sitaramayya died at Vizianagram on 14-3 65 of coronary infarction.

Born on 5-1-1905 Dr. Sitaramayya had his early education in Vizianagram. After completing his studies at the Maharajah's college, he went to study medicine in the Andhra Medical College, Visakhapatnam. He belonged to the first batch of students passing out from this college. After housemanship in the Government Ophthalmic Hospital in Madras and King George Hospital, Visakhapatnam, he started private practice. Later, he joined the service under the Vizianagram Estate in 1936, where he worked for long two decades. Following the abolition of zamindaries in the State, he was offered government service. He was appointed as Assistant Surgeon in which capacity he worked till his retirement in January, 1965.

Dr. Sitaramayya was one of the founder members of the Vizianagram Medical Association, which later converted itself into the Vizianagram Branch of the Indian Medical Association.

He was a grand master of Vizianagram Masonic Lodge, a Rotarian, an executive committee member of the District Branch of the Bharat Scouts and Guides, a member of the Lions' Club and Secretary and Treasurer of the local branch of the Indian Red Cross Society. He was a part time lecturer in health education in the local Training College and also a member of its board of examiners.

His life must have been saddened by the loss of three daughters but till his last days he carried on cheerfully. He was a good family doctor, loved by his patients and respected by his colleagues.

Dr. Irfan Ahmad

Dr. Irfan Ahmad was born in Bhopal on 23-8-41. He passed his Matriculation in 1956 from Jahangiria High School, Bhopal, in the first division. He passed the Intermediate in Science Examination in 1958 from the Government Inter College, Bhopal, and graduated in Medicine from the Gandhi Medical College, Bhopal, in 1963. After completing his rotatory internship of 6 months, he joined on 3-8-64 as a house physician in the department of medicine in the Hamidia Hospital, attached to the Gandhi Medical College.

Dr. Irfan Ahmad

In the last week of March, 1965, he fell ill suffering from infective hepatitis but he continued to attend his duties. On 31-3-65 he had to be admitted in the hospital. Thereafter his condition worsened day by day and ultimately he developed hepatic coma. He breathed his last on 3-4-65 in spite of the best efforts of his colleagues to save his life. He was only 23 years and a few months when death snatched him.

Dr. Ahmad endeared himself to all by his simple living and amiable disposition. 'Smile and let others smile' was his motto. He was an enthusiastic worker of the I.M.A. and was very much liked by his friends and superiors.

Dr. Ahmad leaves behind his old parents, four brothers and three sisters and a large circle of friends and admirers to mourn his loss.

Shri Bodh Raj

Death occurred on 17-9-65 of Shri Bodh Raj, Accountant at the I.M.A. Headquarters, New Delhi.

Shri Bodh Raj joined the Central Office of the I.M.A. in the year 1949, shortly after the shifting of the office to New Delhi from Calcutta. Since then he was attached to the Central Office and served it with singular devotion till his last days. Sometimes he also officiated as Head Clerk-cum-Accountant.

A strong disciplinarian with an unfailing sense of responsibility Shri Bodh Raj attended his duties till 16-9-65 and worked as usual. Next morning at his residence he suddenly collapsed and died of heart failure.

Shri Bodh Raj was a man of amiable nature and cheerful disposition. The warmth and sincerity with which he dealt with one and all who came to him on any business and the patience with which he tackled his diverse tasks in the office endeared him to everybody.

Shri Bodh Raj will be long remembered not only by his friends and colleagues but by all members and office-bearers of the I.M.A. who chanced to meet him either in the I.M.A. Headquarters or during meetings of the Working Committee or the Central Council of the I.M.A.

SUPPLEMENT
Journal of the Indian Medical Association

VOL. 45, NO. 9 CALCUTTA NOVEMBER 1, 1965

BRANCH NOTES

AJMER BRANCH—The 30th annual general meeting was held on the 24-4-65 with Dr. P. D. Mathur in the chair. 43 members attended.

The minutes of the last annual general meeting were read and confirmed. Following this the Hony. Secretary Dr. M. L. Bagh read out the report of the activities of the branch for the year 1964-65.

During the year 1964-65, the branch had eight general and clinical meetings and five executive committee meetings. A large number of members attended the VII Rajasthan State Medical Conference at Bikaner. The branch had the honour of sending the largest contingent of representatives to the Conference among the local branches in Rajasthan.

The clinical meetings arranged by the branch were addressed by distinguished members of the profession. Dr. Handa of the Patiala Medical College was invited to give a talk on Bullous Dermatoses and Superficial Dermatomycoses.

Dr. P. D. Mathur spoke on Coma and its Management and Dr. Rajendra Nath on P. U. O. and Recent Advances in Therapeutics.

Interesting cases were demonstrated and discussed on several occasions. Dr. Kailash Rai presented a case of atresia of the posterior nares and a few cases of submucous fibrosis of the palate and the cheeks. Dr. B. S. Rawat discussed a case of viral pneumonia. Dr. M. S. Mathur presented a case of cerebellopontine tumour and a case of hepatic coma. Dr. G. S. Jhala demonstrated a case of spontaneous pneumothorax treated surgically.

Besides the above clinical cases, interesting films on otorhinolaryngeal examination and anatomy and surgical approach of the hip joint by anterior, posterior and lateral routes were shown at the Western Railway Hospital, Ajmer, by the courtesy of Dr. Amar Chand.

The Hony. Secretary also placed a statement of accounts for the year 1964-65.

Following the adoption of the annual report the President Dr. P. D. Mathur addressed the members. Stressing the great need for unity among the members he said that every member of the medical profession, be he a specialist, a general practitioner, a government doctor, a mission doctor, a railway employee or a private practitioner, should enrol himself as a member of the Association and strengthen its hand. The annual general elections were next held and the following were elected unanimously: President—Dr. J. S. Mathur; Senior Vice-President—Dr. Kunj Behari Lal; Junior Vice-President—Dr. S. D. Ahuja; Hony. Secretary—Dr. M. L. Bagh; Joint Secretary—Dr. Rajendra Nath; Treasurer—Dr. Mrs. Sarla Bagh; Auditor—Dr. H. C. Jain; Representative to the Central Council—Dr. Amar Chand; Representatives to the State Council—Dr. G. S. Jhala, Dr. N. C. Desai and Dr. S. M. Lalla; Members of the Executive Committee—Dr. Mrs. C. H. David, Drs. J. N. Mukherjee, J. A. T. Wells, R. K. Kapoor, B. Manghani, G. L. Kanodia and R. R. Shukla. Dr. J. S. Mathur expressed his thanks to the members for the honour conferred on him and assurred them that he would do his best to make the association meetings lively. The meeting closed with a vote of thanks to the chair.

ANNAMALAIS BRANCH—At the annual meeting held on 24-4-65, the following office-bearers were elected for the year 1965-66: President—Dr. K. Janardhanan; Vice-President—Dr. M. P. Gundappa; Hony. Secretary—Dr. K. P. S. Menon; Hony. Joint Secretary—Dr. P. Devadas.

BANGALORE BRANCH—An extraordinary general meeting was held on 16-4-65 in the M.M.A. Hall, Fort, for nomination of one President and 3 Vice-Presidents for the I.M.A. Working Committee for the year 1965-66. This was followed by a scientific meeting presided over by Dr. M. Authikesavalu. Dr. H. K. Gopalkrishna spoke on Bronchogenic Carcinoma.

A film show was arranged on 21-4-65 in the M.M.A. Hall by courtesy of G. D. Searle and Co. Ltd. The film was on Enovid—10 years of Research on Oral Contraceptives. Dr. Mrs. Christopher gave an introductory talk on the film.

BAREILLY BRANCH—The Republic day 1965 was celebrated on 26-1-65 amidst great jubilation. An interesting programme of sports was arranged in the afternoon. Cricket and hockey were played between service doctors and the private practitioners. The latter won both the matches. In the sports events the ladies' flat race, guava race, mixed musical chair, relay race and the races of the children delighted all present. About sixty doctors of the city including some invitees along with their families participated in the function, which came to a close with tea at the Bareilly College grounds. At night there was a fancy dress parade followed by a variety entertainment programme and a dinner held at Dr. G. S. Dhillon's residence. More than fifty doctors along with their families took part. Prizes were distributed amongst the winners of the sports and the fancy dress.

On 13-2-65 a clinical meeting was held with the President of the branch in chair. Dr. G. K. Srivastava spoke on Low Backache with special reference to Prolapse Disc.

An urgent meeting of the Executive Committee was held on 23-2-65 with Dr. A. D. Bhandari in the chair to settle the controversy given rise to between two members of the Association following a case of electrocution. After some discussion a resolution was passed proposing the formation of a sub-committee which should arrange an honourable compromise between the parties.

On 13-3-65, a meeting was held with Dr. Bhandari in the chair. Lt. Col. S. C. Kapoor, a specialist from the Military Hospital, gave a talk on Coronary Artery Disease. He dealt mainly with the atheromatous conditions of the coronary artery and discussed in detail Angina and the Myocardial Infarct. The talk was followed by a discussion in which many members took part.

The Executive Committee met on 9-4-65 with Dr. Bhandari in the chair. The Secretary announced that by courtesy of the District Hospital authorities the meeting hall had been renovated and now it needed furnishing. It was therefore decided by the Committee to take immediate steps for the purchase of furniture.

There was a discussion on the bulletin of the branch. It was decided to secure maximum advertisements and collect contributions of high standard, for the bulletin. It was also decided that in arranging farewells to transferred members austerity should be observed in the matter of expenses and that a week's notice must be given to the Secretary.

A clinical meeting was held on 10-4-65. Dr. J. S. Makhani of the Mission Hospital, Bareilly, spoke on Orthopaedic Management of the Post-Polio Paralysis. He said that polio was not limited to the infants and that the orthopaedic surgeon must be associated with the case from the very start. The same surgeon should preferably treat the case up to the adult age, he said. He illustrated the orthoroentgenogram and its usefulness. He gave an idea of placental graft in the treatment of this disease and described many manoeuvres of arthoplasty and arthodesis.

BOMBAY TERRITORIAL BRANCH—The following office-bearers were elected in the annual meeting of the branch and requested to take over charge of the office with effect from 24-4-65: President—Dr. Shantilal C. Sheth; Vice-Presidents—Dr. V. K. Toraskar and Dr. J. M. Kotwal; Hony. Secretary—Dr. M. A. Panwala; Hony. Joint Secretaries—Dr. K. M. Thakar and Dr. S. S. Ajgaonkar.

CANNANORE BRANCH—A clinical meeting was held at the Military Hospital Cannanore, on 16-5-65 with Dr. P. I. Jacob, President, in the chair. 30 members attended.

The President in his introductory speech informed the members about the transfer of Dr. K. Mukundan, Treasurer of the branch, to Palghat.

Dr. M. K. Balakrishnan Menon was elected Treasurer in place of Dr. K. Mukundan.

Dr. P. U. Joseph was elected to the State Working Committee as a member from this branch in place of Dr. Mukundan.

Dr. T. T. Thomas gave a lecture on Swellings of the Breast. The lecture was followed by discussions in which many members took part.

The Hony. Secretary thanked Dr. Mukundan for the help he rendered to the branch as Treasurer and Major H.R. N. Moorthy for the tea-party and arrangements for the meeting at the Military Hospital. He also thanked Dr. Thomas for the talk.

CHAIBASA BRANCH — A meeting was held on 25-4-65 at the residence of Dr. K. P. Bakshi. 16 members were present.

Dr. M. N. Sardana of I.I.S. Co. Hospital, Gua, took the chair.

The proceedings of the last meeting were confirmed.

The letters and circulars received from the State Branch and the Central Office were read and discussed. The name of Dr. M. K. Sharma of the branch was proposed for the office of Vice-Presidentship of the State Branch for the year 1965-66.

The following resolution was passed unanimously:

It is resolved unanimously that in case the Government accepts resignations of the Government Medical Officers no member of the I.M.A. Chaibasa branch will offer to work in the hospitals as a stop-gap arrangement.

Dr. P. K. Mitra was elected librarian for the year 1965-66 and was requested to take necessary steps for the efficient functioning of the library.

Two cases of clinical interest were presented by Dr. J. S. Sinha and Dr. N. K. Sen Gupta.

The case presented by Dr. Sinha was of an old lady of 60 years who was having recurrent haemoptysis for the last one year. A.F.B. in sputum was found negative on repeated examinations and she was fever free. On x-ray examination, a big potato size opacity was found in the pesterior part of the basal portion of the left lung, separate from the liver. The differential diagnoses of cysts (congenital and hydatid) and lung abscess were discussed by other members.

The other case presented by Dr. N. K. Sen Gupta was that of a huge splenomegaly in a boy of about 15 years. The boy was severely anaemic. The differential diagnoses of Banti's Syndrome, Acholuric Jaundice, Kala-azar (as the boy was getting fever off and on), Aleukaemic Leukaemia and Haemoglobinopathies as well as Cooley's anaemia were discussed by different members.

The meeting closed with a dinner for which Dr. K. P. Bakshi was the host.

DELHI STATE BRANCH— At the annual general meeting held on 12-4-65, the following office-bearers were elected for the year 1964-65: President—Dr. G. D. Dhala; Vice-President—Dr. Santokh Singh; Hony. Secretary—Dr. K. L. Tuli; Joint Secretary—Dr. P. Raj Monga; Assistant Secretary—Dr. Bhim Sen Bansal; Treasurer—Dr. Rajinder Nath; Librarian—Dr. N. S. Banerji.

DHANBAD BRANCH—A meeting was held on 3-12-64 at the Town Hall, Dhanbad, with Dr. S. N. Ghosh in the chair.

At the outset the meeting condoled the sad demise of Dr. T. A. Narayanam. Feeling references were made by several speakers to his charming personality, amiable nature, humane approach, professional efficiency and ethics. Major H. C. Mullick, Drs. B. N. Hazra, A. K. Chatterjee and Major D. D. Mitra spoke highly about the qualities of his head and heart and recalled their memories of personal relations with him.

The following resolution was then moved by the President:

This amergent meeting of the Indian Medical Association, Dhanbad branch, records its profound sorrow at the sad and untimely demise of Dr. T. A. Narayanam, an active member and ex-Vice President of the branch on the morning of the 1st December, 1964, and offers its heartfelt condolence to the members of the bereaved family. Dr. Narayanam was a man of very amiable and helpful nature. He endeared himself to all by his charming personality and professional integrity.

All members stood in silence for two minutes to pay homage to the departed soul.

It was decided to celebrate the Silver Jubilee of the branch sometime in March, 1965, in a befitting manner and the following sub-committees were formed with powers to co-opt members, if necessary: Finance Sub-Committee—Dr. Dr. S. N. Ghosh, *Convener,* Dr. P. K. Dutta, Rajendra Prosad, P. P. Goel, M. Mishra, Major H. C. Mullick and B. N. Hazra; Souvenir Sub-Committee —Dr. M. N. Dey, *Convener,* Drs. S. N. Ghosh, P. P. Goel and M. M. Saha; Symposium Sub-Committee—Dr. A. K. Chatterjee, *Convener,* Drs. A. K. Bhattacherjee, P. P. Goel and S. Mukherjee; Health and Exhibition Sub-Committee—Dr. M. Mishra, *Convener,* Drs. M. N. Dey, D. N. Chatterjee (Sindri), Major D. D. Mitra, Drs. Rajendra Prasad and S. N. Ghosh.

The Hony. Secretary placed before the house a proposal from Shri Rasik Lal Worah, Managing Trustee of the Lakshmi Narayan Trust, regarding the joint venture of the I.M.A. and the Trust for organising medical relief as was done last year. A sub-committee was formed which was entrusted to take up a suitable scheme and go ahead with it. The sub-committee consisted of the President and the Hony. Secrretary of the branch, Major H. C. Mullick, Dr. Rajendra Prasad and Dr. P. P. Goel.

The meeting terminated with a vote of thanks to the chair.

DIBRUGARH BRANCH—The annual general meeting was held on 30-4-65 in the Pharmacology Department, Assam Medical College, Dibrugarh. Dr. M. N. Bhattacharyya, President of the branch took the chair. 8 members were present.

The following office-bearers were elected unanimously for the year 1965-66: President—Dr. M. N. Bhattacharyya; Vice-Presidents—Dr. S. N. Dutta and Dr. A. M. Rahman; Hony. Secretary—Dr. R. M. Deb Roy; Hony. Joint Secretary—Dr. D. N. Bhagaboti; Executive Committee Members—Drs. S. C. Barooah, R. Goswami, S. K. Baruah, K. L. Ghosh and J. Choudhury.

The meeting considered the question of revision of the subscription rate and decided that the subscription payable by the local branch should be raised from Rs. 2/- to Rs. 3/- per annum. It was hoped that this step would raise the total annual subscription from Rs. 13/- as at present to Rs. 14/-. The proposal was to be effective from the Association year 1965-66 which is to begin from 1-10-65.

It was also decided to send intimation of the change of office-bearers to the United Bank of India to enable the present Hony. Secretary to operate the account standing in the name of the branch.

It was decided to entrust the organisation of the Refresher Course for General Practitioners, which was sponsored by the branch, to the Assam State Branch to be conducted by a committee with Dr. S. C. Barooah as the General Secretary and Dr. R. Goswami as the Organising Secretary. The State Branch was also requested to invite doctors from all over the state to participate in the Refresher Course. The meeting decided to forward its new proposal for Refreshers Course to the I.M.A. Headquarters and seek their approval.

The meeting decided to nominate Dr. Shantilal C. Sheth of Bombay for the Presidentship of the I..MA. for 1965-66.

The meeting closed with light refreshments for the members and a vote of thanks to the chair.

DURG BRANCH —The following office-bearers were elected at the annual general meeting held on 15-3-65: President—Dr. W. W. Patankar; Vice-President—Dr. B. K. Chatterjee; Hony. Secretary—Dr. R. Siddiqui; Joint Secretary—Dr. I. P. Dixit; Members of the Executive Committee—Dr. T. P. Niyogi, Dr. S. P. Sahu and Dr. Mrs. M. George.

ERODE BRANCH —The annual meeting was held on 28-2-65. At the outset the following office-bearers were elected for the year 1965-66: President—Dr. B. S. Viswanathan; Vice-President—Dr. N. S. K. Swamy; Hony. Secretary—Dr. P. K. Krishnamurthi; Assistant Secretary —Dr. Smt. Badrunissa; Treasurer—Dr. M. Mukunda Shenoy; Representative to the Central Council—Dr. K. Balasubramanyam; Representatives to the State Council —Dr. M. Narayana Shenoy and Dr. L. K. Muthuswami.

Following the election of the office-bearers a clinical session was held with Dr. P. K. Kalyanaraman, Hony. Physician, Government Hospital, Coimbatore, in the chair. Dr. R. Subramanyam, Professor of Medicine, Madras Medical College, and Physician, Government General. Hospital, Madras, spoke on Some Aspects of Cirrhosis of Liver and Management.

Dr. Smt. E. V. Kalyani, Hony. Obstetrician and Gynaecologist, Government Hospital for Women and Children, Egmore, Madras, spoke on Recent Trends in the Practice of Obstetrics.

Dr. R. S. Mahale, Reader in Obstetrics and Gynaecology, Kasturba Medical College, and Hony. Assistant Medical Officer, Lady Goschen Hospital, Mangalore, spoke on Common Obstetric Problems.

Dr. M. Viswanathan, Hony. Professor of Clinical Medicine, Stanley Medical College, and Hony. Physician in charge of Diabetic Clinic, Government Stanley Hospital, Madras, spoke on Diabetes Mellitus and its Management.

The meeting concluded with a vote of thanks proposed by the Hony. Secretary, Dr. P. K. Krishnamurthi.

FAIZABAD BRANCH —A meeting of the Scientific Section of the branch was held on 17-4-65 in the District Hospital. A film show and a tea party were arranged by Sandoz (India) Ltd. The programme was continued on 18-4-65 at the resdence of the Civil Surgeon. On 19-4-65, a film show was arranged in the local Women's Hospital for the benefit of nursing trainees and staff of the hospital. The films were about normal and complicated deliveries.

A meeting was held in the premises of the Mission to Lepers on 23-4-65. Dr. P. C. Tandon took the chair.

The circulars received from the State Branch and the Central Office were read. Nominations for the President and 3 Vice-Presidents—both for the I.M.A. Central and for the State Branch—were finalised. A public Relations Committee was formed on the lines suggested by the State Committee. Dr. Mrs. C. Patrick entertained the members to a dinner.

The meeting closed with a vote of thanks to Dr. Mrs. Patrick and the chair.

GUJARAT STATE BRANCH —At the annual meeting of the State Council held at Anand on 30-4-65, the following members were elected representatives to the Working Committee of the I.M.A. for 1965-66: 1. Dr. C. P. Munshi, 2. Dr. P. R. Trivedi; Alternate Representatives—1. Dr. M. S. Bhatt, 2. Dr. I. G. Bhatt.

HASSAN BRANCH —A meeting was held on 26-4-65 at the S. C. Hospital, Hassan.

The Hony. Secretary Dr. B. M. Narayana made an introductory speech following which the meeting proceeded to fill in by election the office of the President which had fallen vacant due to the retirement of Dr. M. C. Devanniah, District Surgeon, from service. Dr. B. M. Narayana, whose name was proposed by Dr. V. N. V. Pathy and seconded by Dr. Bore Gowda was unanimously elected as President for the remaining period of the session 1964-65.

The name of Dr. B. Chakrapani Iyengar was respectively proposed and seconded by Dr. Nagaraja Rao and Dr. H. Chandrasekharappa for the post of Vice-President of the branch. The proposal was unanimously carried.

Dr. H. S. Ramachandran proposed the name of Dr. H. Chandrasekharappa for carrying on work as Secretary for the remaining period of the session in place of Dr. B. M. Narayan. The proposal, which was seconded by Dr. S. Nanjappa, was unanimously passed.

Following the elections Dr. T. V. Shamanna presented a case of abscess lung and Dr. H. S. Ramachandran a case of inguinal hernia in which contents of the sac was the large intestine. Many members took part in the discussion that followed.

The circular no. 28/64-65 dated 18-1-65 received from the IMA headquarters was considered. It was resolved that the doctors who had not yet enrolled themselves as members might be permitted to do so on paying half-year's subscription only.

INDORE BRANCH —A monthly clinical meeting was held on 20-3-65. Dr. G. A. Kher was in the chair. Dr. N. R. Bhandari presented the case of a boy aged 10 years with undescended testis (left side) and lump in the abdomen with secondary metastasis in lungs, excretion pyelography from the lump showing malignant cells. The patient satisfactorily improved on treatment with endoxan. A case of traumatic arteriovenous fistula of femoral artery and a case of adenocarcinoma of the colon in a child were presented by Dr. K. L. Bandi. Dr. V. K. Agarwal presented few cases of rhinoplasty using homogenous cartilaginous grafts with good results. Dr. Dwivedi presented radiological features of cases of chronic recurrent volvulus of stomach and said that this condition was not uncommon and stressed the importance of doing barium study to diagnose the condition when the patient was in pain.

JAGATDAL BRANCH —A meeting was held on 6-3-65. 38 members were present. Circulars received from the State Branch were read and discussd. The draft reply to the questionnaire regarding the working of E.S.I. Scheme was considered. The draft was approved and referred back to the State Branch. Dr. R. R. Bhattacharjee narrated his experiences of the Annual State Medical Conference held at Bolpur and also gave a summary of the proceedings of the Council meetings. The branch was represented by Drs. P. Sinha, T. P. Chatterjee, R. R. Bhattacharjee and P. K. Dass, besides Dr. I. B. Ganguly and Dr. Patra who attended as Reception Committee members. Discussions took place about the opening of the new office room on 14-4-65. Dr. Sthanpati, Dr. S. P. Bandopadhyaya and Dr. H. P. Roychowdhury were authorised to make necessary arrangements.

A meeting was held on 27-3-65. Circulars received from the Central Office and the State Branch and the proceedings of the State Council Meeting were read and noted. The questionnaire on Family Planning Scheme was read and discussed. Dr. (Mrs.) Ruby Biswas was authorised to go through the questionnaire and draft the answers. The working of the E.S.I. Scheme in this area also came up for discussion in the meeting.

A general meeting was held on 14-4-65. 45 members were present. The office room of the branch was opened by Dr. Susil Chakravarty, one of the senior-most members. Shri G. B. Ghose was present as the chief guest. Dr. H. P. Roychowdhury and Sri provas Roy entertained the audience with songs and Dr. Mondol played on guitar. Dr. T. K. Ghose recited a poem suited to the occasion. Many veteran members, who were present, spoke expressing their pleasure on this happy occasion. The members and the guests were treated to tea and refreshments.

The death of Dr. B. N. De, an old member of the branch, was mourned at a meeting held on 29-4-65. A resolution was passed following which the members stood in silence to pay homage to the deceased. It was decided to send a copy of the resolution to the bereaved family.

Circulars received from the Central office and the State Bracnch were then considered. Proceedings of the meeting on Shops and Establishments Act were also read and discussed.

JALPAIGURI BRANCH—The annual general meeting was held on 6-3-65 and 7-3-65 at the Bamandanga Tea Estate (Birendra Chandra Tea Estate). 30 members were present. Dr. C. C. Sanyal, President of the branch, took the chair.

The Hony. Secretary Dr. H. M. Hore placed the annual report for the session 1963-64.

The branch had 53 members at the beginning of the session. The number was 50 at the close of the session, 5 members having left the town on transfer and 2 doctors having joined as new members.

The branch held 22 meetings, in all, during the year, including 9 executive committee meetings and 2 scientific meetings. It organised condolence meetings on the demise of Capt. S. C. Ghose, Dr. Bhabani Mohan Dutta—both members of the branch, Dr. H. K. Roy, President of the Bengal State Branch and Pandit Jawaharlal Nehru, the Prime Minister of India. A symposium on Malnutrition was the main feature of a scientific meeting held at the Anandapur Tea Estate. In the other scientific meeting Dr. M. M. Das spoke on Peptic Ulcer.

The branch organised for the members a Bijoya Sammilani, a film show by courtesy of Dey's Medical Stores Ltd., and an auction bridge tournament.

The above report was unanimously adopted in the meeting. The audited statement of accounts for 1963-64 was also passed. The following office-bearers were then elected for the session 1964-65: President—Dr. C. C. Sanyal; Vice-Presidents—Dr. J. N. Maitra and Dr. D. L. Lahiri; Hony. Secretary—Dr. Satyendra Nath Majumdar; Assistant Secretaries—Dr. M. Roy and Dr. G. L. Kundu; Auditor—Dr. K. C. Saha; Members of the Executive Committee—Drs. A. D. Guha Neogi, H. M. Hore, Capt. M. K. Moitra, Drs. S. Sen Gupta, K. R. Paul, S. K. Bagchi and N. L. Ghose; Representative to the Central Council—Dr. S. K. Bagchi; Representatives to the State Council—Dr. S. N. Majumdar, Dr. C. C. Sanyal and Dr. S. P. Chatterjee.

In the scientific session arranged on this occasion, besides members of the branch, a number of doctors from the surrounding tea gardens participated. Dr. C. C. Sanyal conducted the business of the session. Dr. M. M. Das spoke on Cholelithisis. A lively discussion followed the talk. A symposium was also arranged on Psychoneurosis in General Practice. Capt. M. K. Moitra initiated the discussion. Dr. D. C. Dutta spoke on Psychoneurosis in Obstetrics and Gynaecology. Dr. N. C. Ghose spoke on Psychoneurosis in Ear Diseases. Dr. D. Ganguly spoke on Psychoneurosis in Eye Diseases. Dr. S. K. Bagchi and Dr. A. D. Guha spoke on Psychoneurosis in General Practice.

Dr. Sanyal summed up the discussions.

KATIHAR BRANCH — On 7-3-65 before a distinguished gathering in the Town Club premises the Bihar Health Week was inaugurated by Sri I. K. Saran, S. D. O., Katihar. Dr. B. N. Prasad presided over the function. In the absence of Dr. P. C. Mitra, Hony. Secretary, Dr. G. N. Mukherjee explained in brief the significance of the observance of the Health Week. Sri B. G. Gupta, Principal, Women's College, Sri B. N. Sinha, Principal, D. S. College and Dr. T. K. Jha also addressed the gathering. Inaugurating the Health Week Sri Saran assured his cooperation in all campaigns for health in the Katihar Town and sub-division.

During the week, health films were shown and popular lectures on health given at Durgasthan, Seamapur, Manshahi and the rural areas of Manihari. The Public Relations Department of the Government extended its full cooperation in making this programme a success.

The drive for vaccination and inoculation was launched in several areas. 225 persons were given smallpox vaccination and 400 persons were inoculated against cholera. 114 wells were also disinfected.

Health examination of school students and community health survey were undertaken at Seamapur.

A baby show was organised in the Town Club where healthy babies were given prizes. Consolation prizes were given to other babies.

A clinical meeting was arranged at Manihari which was attended by the local medical practitioners. A number of interesting cases was demonstrated and these were followed by discussions in which many enthusiastically took part.

A meeting was held on 28-3-65 with Dr. B. N. Prosad in the chair. Most of the members were present. Dr. T. K. Jha spoke on Hypertension and its Management. The meeting concluded with a film show on Cardiac Message arranged by the courtesy of Smith Kline & French (India) Ltd.

The World Health Day was observed by the branch on 7-4-65 with Mr. I. K. Saran, S.D.O. in the chair.

Dr. G. M. Mukherjee, Dr. P. Bhattacherjee, Dr T. K. Jha and Mr. S. Saran spoke about smallpox and its various aspects.

The meeting also decided to launch a drive for inoculation and vaccination against cholera, typhoid and smallpox, in cooperation with the North Block, Katihar, on 2-5-65 at Budhurchak, a village adjoining Katihar.

MADURAI BRANCH—The monthly meeting for April was held on 10-4-65 under the chairmanship of Dr. C. K. Padmanabha Menon, President of the branch. The Hony. Secretary, Dr. T. Thirugnanam read out the minutes of the previous monthly meeting held on 13-3-65. Dr. D. Bhupathi, Reader in Medicine, Madurai Medical College, and Physician, Erskine Hospital, Madurai, gave a talk on Medical Management of Peptic Ulcer. The Hony. Secretary proposed a vote of thanks following which the meeting terminated.

MANDVI KUTCH BRANCH—A clinical meeting was held at Vithalwadi on 1-5-65. Medical men from different parts of the district attended the meeting.

Dr. Ramesh S. Shah, Cardiologist and Dr. Anil Baxi, Thoracic Surgeon, were present as guests.

Dr. Shah spoke on the Management of a Cardiac Patient.

Dr. Baxi spoke on the Surgical Management of Pulmonary Tuberculosis. The talk was followed by a film show and a dinner arranged by courtesy of Sandoz (India) Ltd. The following films were screened: (1) Methergine. (2) Peritoneoscopy in Gynaecology. (3) Cor pulmonale.

A vote of thanks was proposed by Dr. C. J. Mehta.

MOTIHARI BRANCH—An ordinary meeting was held on 25-4-65 at the residence of Dr. Manzoor Ahmad of the Sugauli Sugar Factory. Dr. Hari Shankar Prasad took the chair. 13 members were present.

At the outset the sad demise of Dr. N. C. Sircar was condoled and one minute's silence was observed as a mark of respect to the departed soul. A resolution was passed conveying the sympathy of the members to the bereaved family.

The proceedings of the last meeting were then read and confirmed.

Dr. Jagdish Prasad of Ramgarhwa was enrolled as a new member.

The letters received from the State Branch and the Central Office were read and discussed. Dr. A. K. Sen's letter regarding membership drive was also placed. The Secretary and the members agreed to contact all the medical practitioners of the area in person and pursuade them to join the Association.

A clinical talk on Hypertension and its Management was given by Dr. Hari Shanker Prasad. Dr. M. Alam discussed the role of surgery in the treatment of hypertensive cases. All the members participated in the discussions that followed.

An interesting x-ray of spine in which the L5 vertebra fused with the sacrum was shown to the members who discussed the same.

The case of a baby with Post-Encephalitic Parkinsonism was also presented to the members.

Dr. Ahmad entertained the members present to a dinner.

SAGAR BRANCH —A meeting was held on 9-4-65 at the Military Hospital. Two films on Physical Diagnosis were shown by courtesy of Ciba Ltd. Dr. Makhanlal proposed a vote of thanks to Mr. Kumar, Sales Manager, Ciba, for arranging the film show.

A meeting was held on 27-4-65 in the Recreation Hall in the Military Hospital campus.

Lt. Col. S. C. Sachdev, Surgical Adviser to the Central Command, was present as the chief guest. Dr. Makhanlal presided over the meeting.

Dr. S. C. Chowdhary, Hony. Secretary, read out the minutes of the last meeting, which were confirmed.

A case of spine bifida, a case of renal tuberculosis, a case of compression paraplegia, a case of diaphyseal exostosis and a case of T.B. glands axilla were presented for discussion. Lt. Goyle, Capt. Chattopadhya, Dr. M. L. Shukla, Maj. Y. P. Mehta and Lt. Col. S. C. Sachdeva took part in the discussions.

This was followed by a tea party arranged by the O. C. Military Hospital.

SALEM BRANCH —An ordinary meeting was held on 25-4-65 at the Foulke's Hall.

The minutes of the last annual meeting and the Executive Committee meeting held on 18-4-65 were read by the Hony. Secretary.

The meeting discussed the preparations for the 19th Madras State Medical Conference and formed various sub-committees for organising the Conference. Some members who were specially invited for this purpose gave their suggestions. Following this the Treasurer read the statement of accounts for January, 1965.

The President, Dr. K. Jayaramachandran introduced the guest speaker Dr. K. N. Vasudeva, Professor of Operative Surgery, Madras Medical College and Surgeon, Government General Hospital, Madras. Then he read a letter received by him from Dr. S. Raju Ayyar, President, Ramnad Branch, requesting him to give them the pleasure of holding the 19th Madras State Medical Conference at Srivilliputtur. The members agreed to comply with this request.

Dr. K. N. Vasudevan addressed the members on the Significance of Urological Symptoms and Findings and on Clinical Cocktail. He illustrated his speech with the help of several x-ray pictures.

The meeting concluded with a vote of thanks by the Hony. Secretary Dr. Kumari B. Mukambu.

SHAHABAD BRANCH – A regular monthly meeting was held on 29-11-64 at the residence of Dr. B. M. Sinha 21 members were present.

The confirmation of the proceedings of the last meeting was put off for the next meeting on the request of the Secretary as the report had not been ready by that time.

The statement of audited accounts for the year 1963-64 was read by the auditor and it was passed by voice vote. All the members expressed their satisfaction at the statement.

Dr. B. M. Sinha was unanimously elected representative to the State Council in place of Dr. S. M. Shamim Ahmad.

It was decided to send a letter of thanks to Dr. J. C. Patel of Bombay for his illuminating speech at the 24th Bihar State Medical Conference at Arrah.

It was also resolved that the members intending to attend the All-India Medical Conference at Kakinada should contact Dr. K. K. Saran.

Dr. B. M. Sinha entertained the members to tea following which the meeting came to a close.

A monthly meeting was held on 27-2-65 at the residence of Dr. A. Prasad. Twenty members were present.

The minutes of the previous meeting were confirmed.

Members willing to attend the World Health Conference at England were requested to contact the Hony Secretary.

Dr. K. N. Pathak gave a talk on Clinical Observation on Gastric Perforation. Drs. R. Sinha, K. K. Sinha, J. Sahai and Dr. Miss K. Dongre took part in the discussions. Dr. J. Sahai and Dr. Miss Dongre narrated their own experiences on the subject. Dr. Pathak suitably answered the queries made by the members.

A resolution was passed recommending the closure of the old account of the branch with the local Bank of Bihar opened in the name of the Shahabad District Medical Association (Branch of the I.M.A., Arrah) and reopen it in the name of Indian Medical Association, Shahabad Branch, Arrah. It was resolved that this account should henceforth be operated by the Secretary, Dr. B. M. Sinha and Treasurer, Dr. S. M. Shamim Ahmad.

A monthly meeting was held on 30-1-65 at the residence of Dr. B. P. Lal. The minutes of last meeting were confirmed.

It was unanimously resolved that the membership fee be raised from Rs. 13/- to Rs. 15/-.

Dr. A. Prasad gave a talk on Tetanus. He thoroughly discussed the subject from different aspects. A number of members took part in the discussion. Dr. A. Prasad suitably replied to the queries. The host Dr. B. P. Lal entertained the members to refreshments.

A monthly meeting was held on 26-12-64 at the residence of Dr. R. Sinha. The minutes of the last two meetings were conrfimed. Dr. L. R. Dongre, President of the All-India Tuberculosis Association, was present as the chief guest. He gave a talk on Modern Trends in Tuberculosis. Dr. Dongre thoroughly discussed and explained the advantages and disadvantages of the latest Anti-T.B. Drugs. Dr. K. K. Sinha, Superintendent, Koilwar Sanatorium, initiated the discussion on the various aspects of the disease followed by Doctors B. N. Jha, S. M. Shamim Ahmad, A. Prasad, S. N. Bhagat, R. B. Chowdhary and Khublal Ram. Dr. Dongre suitably replied to the points raised during the discussions.

It was decided to celebrate the Bihar Health Week. A Health Week Committee was formed with the District Magistrate, Shahabad, as President, Dr. R. Sinha as Chairman, Dr. B. M. Sinha as Secretary and Dr. R. B. Chowdhury as Joint Secretary. A sub-committee for the Health Week was formed with the following members: Doctors B. N. Jha, K. K. Sinha, V. Shankar, K. Prasad, S. N. P. Bhagat, J. Mishra, H. N. Singh, K. Dongre, S. M. Shamim Ahmad, N. N. Sinha, D. D. Kalwar.

The branch observed the Health Week on March 7-14. This year, instead of urban areas, three villages, namely, Chotaki Sanadia, Piru and Koilwar, were chosen for working out the programme of the Health Week. In village Chotaki Sanadia a smallpox inoculation centre was opened and quite a large number of children was inoculated against smallpox. On 7-3-65 a baby show was organised. 12 prizes were distributed to the winning babies under different age groups. Sweets, balloons and lemon-drops were distributed to all the children present on the occasion. In all, 60 children took part in the competition. The Rotary Club, Arrah, actively associated itself with the programme and donated Rs. 50/- towards the expenses. The President of the Rotary Club, Mr. Huda gave away the prizes.

On 8-3-65 the Health Week was inaugurated in the campus of the Arrah Sadar Hospital by Shri A. Q. Ansari, Minister for Health, Bihar. Popular lectures on family planning, National Malaria Eradication Scheme, smallpox and leprosy were delivered by distinguished doctors before a vast gathering. Dr. Lala Surajnandan Prasad, Dr. Jamuar, Secretary, Bihar Health Week Committee and Dr. P. N. Sinha, M.L.C. came all the way from Patna to participate in the inaugural function. A team of doctors formed with the members of the branch moved round the different villages under the nighbouring blocks for giving the people inoculation against smallpox and cholera.

In the Arrah subdivison the number of persons given primary vaccination was 2228 and that of persons given re-vaccination 16,320. 24,238 people were inoculated against cholera and 2265 wells were disinfected.

A group of members went to the local Mahajani School on 12-3-65 and examined 244 boys out of whom 17 boys were referred to Arrah Sadar Hospital for specialised treatment.

A few cases of vasectomy were done at Piru and also in Arrah Sadar Hospital during the week. As an impetus to the workers of the Arrah Municipality to keep thier wards clean, prizes were awarded to the sanitary staff for manitaining cleanliness. Ward No. 17 was declared the cleanest ward by the judges. The running trophy for maintainng a high standard of sanitation went to the Zilla School.

A District Medical Conference comprising all the branches of the I.M.A. in the district of Sahabad was held in the premises of the T.B. Sanitorium, Koilwar, on 14-3-65. There was a panel discussion on Peptic Ulcer. Dr. K.K. Sinha acted as the moderator. The participants were Drs. J. N. Singh, A. Prasad, J. P. Sinha, J. Sinha, K. N. Pathak, M. Mishra, J. Sahay and M. Prasad.

Besides the speakers over 60 doctors from various parts of the district attended the Conference. The discussions lasted for about 6 hours. All those present were treated to refreshments and served with lunch. Dr. K. K. Sinha and his staff were all attention to the guests.

Shri A. Hakim, District Magistrate, Shahabad, next gave away the prizes and trophies to the winners in the various competitions held during the Health Week.

The Conference was followed by a meeting of the District Medical Services Association under the presidentship of Dr. R. Sinha, Civil Surgeon, Shahabad.

A resolution was passed in the meeting condemning the inhuman and insulting treatment meted out to the doctors and staff of the Sadar Hospital, Dhanbad, and recommending the setting up of a one man commission of enquiry with a senior High Court Judge to go into the whole sordid episode.

SRIKAKULAM BRANCH—Under the auspices of College of General Practitioners, Hyderabad, the branch held a a Refresher Course on April 10-11 under the presidentship of Dr. T. Narayana Reddy, District Medical Officer. The lectures delivered for the Refresher Course were attended by most of the members of the Srikakulam and the Parvatipuram branches and also by some doctors from Parlakimidi.

On 10-4-65 Dr. S. Sreenivasulu Reddy, Additional Professor of Surgery, Andhra Medical College, Visakhapatnam, spoke on Rationale of Treatment of Duodenal Ulcer and Dr. K. Krishnamurthy, Additional Professor of Medicine of the same College spoke on Cardiac Emergencies.

On 11-4-65 Dr. P. Kotaiah, Professor of Tuberculosis, Andhra Medical College, Visakhapatnam, spoke on Pitfalls in the Diagnosis of Tuberculosis and Latest Trends in the Diagnosis of Tuberculosis. Dr. K. Krishnamurthy spoke on Acute E.N.T. Diseases. The participants could also listen to tape-recorded lectures made available by the courtesy of the College of General Practitioners.

The members were entertained to a dinner by the branch and to a lunch by Drs. T. Joga Rao and K. Viswanathan.

Dr. B. V. J. Somayajulu, Hony. Secretary, appealed to the members for funds for constructing a permanent building of the branch. The members generously responded by donating towards the building fund their travelling allowance and dearness allowance.

A meeting was held under the presidentship of Dr. B. L. K. Sastry on 8-5-65 in the absence of Dr. T. Narayana Reddy.

Dr. T. R. Seshagiri Rao, Professor of Radiology, Andhra Medical College, Visakhapatnam, spoke on Common Radiological Examinations. He demonstrated a number of x-ray slides and discussed the common pitfalls.

The partners of Srikakulam X-Ray and Diagnostic Clinic were 'At home' to the members.

Dr. B. V. J. Somayajulu, Hony. Secretary, proposed a vote of thanks to the host.

XXX U. P. STATE MEDICAL CONFERENCE : : NAJIBABAD : : 1965

Dr. Bhola Nath, Hony. Secretary, I.M.A., U.P. State Branch informs:

The 30th U.P. State Medical Conference will be held at Najibabad in the district of Bijnor on November 21-22, 1965. Dr. K. P. Tiwari, President and Chief Medical Officer, Vallabh Ram Salig Ram Charitable Hospital, Varanasi, will preside over the Conference. All members of the medical profession in U.P. are cordially invited to join the Conference and make it a success. They are also requested to take keen interest in the scientific session, which is being organised on this occasion. For further information communications should be addressed to the Organising Secretary, Dr. N. S. Saxena, Iqbal Niket, Najibabad, Bijnor District, U.P.

BIHAR STATE MEDICAL CONFERENCE POSTPONED

Dr. P. N. Sinha, Chairman, Silver Jubilee Celebrations Committee, Bihar State Medical Conference, Patna, 1965, announces:

The Silver Jubilee Session of the Bihar State Medical Conference has been postponed due to the national emergency.

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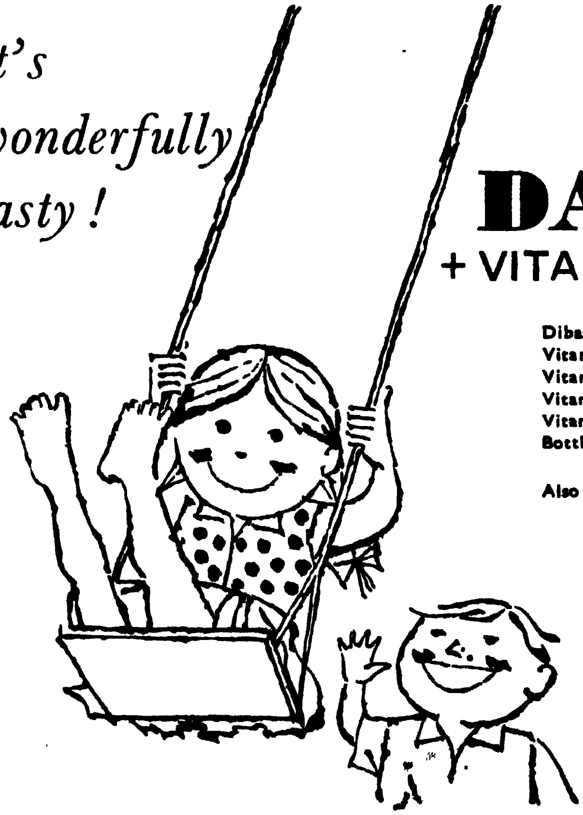

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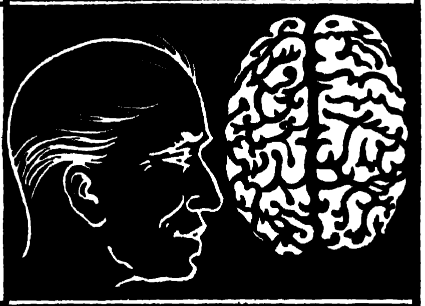

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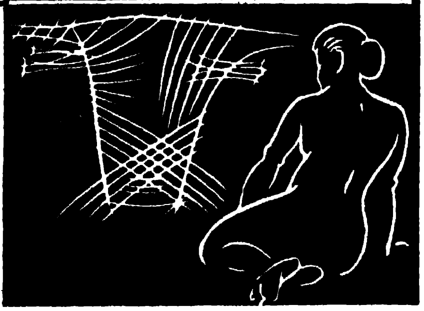

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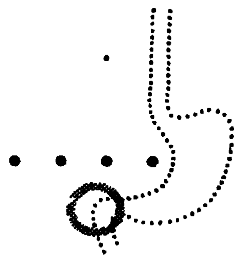

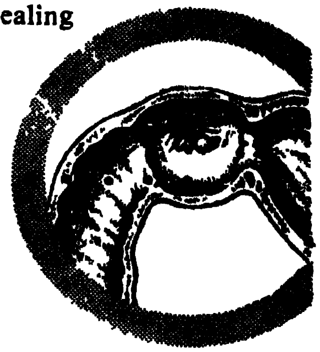

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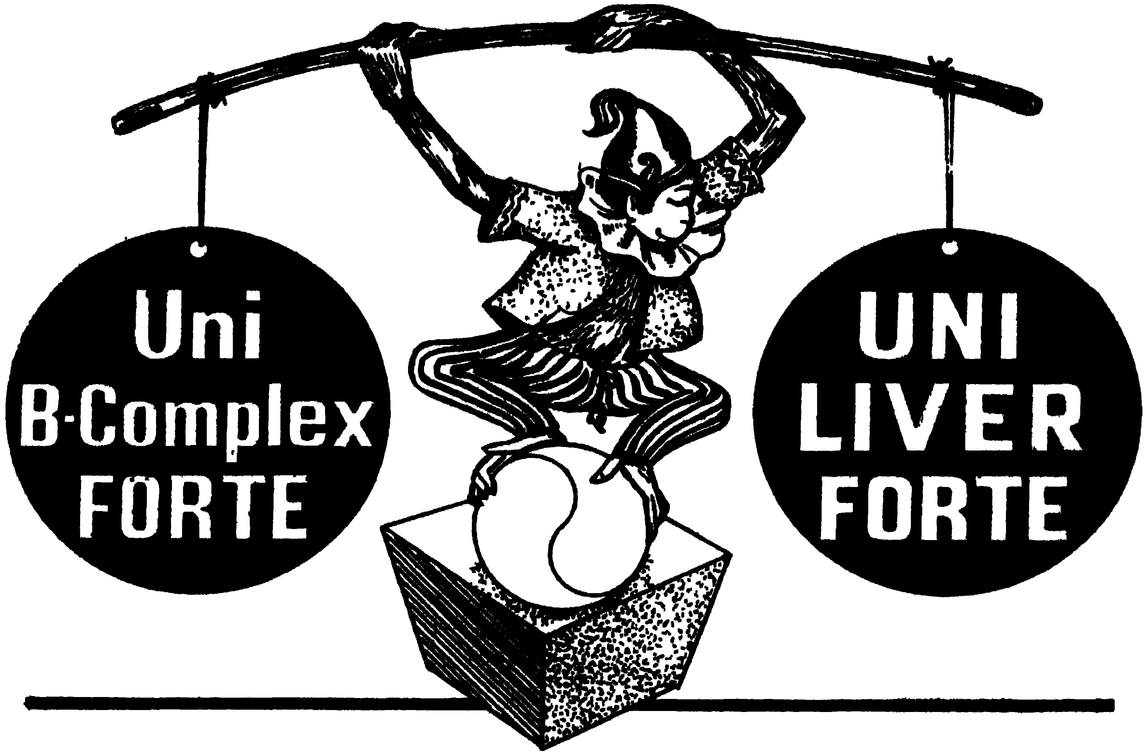

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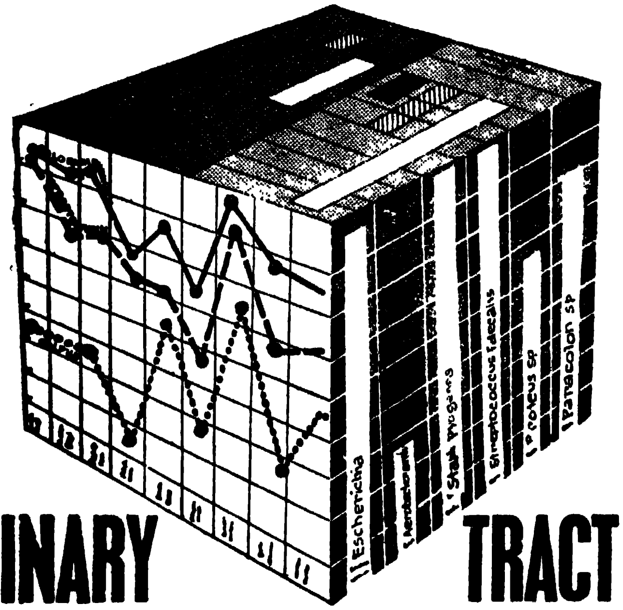

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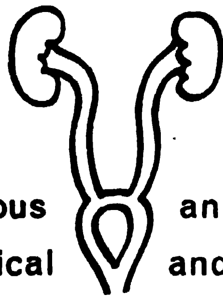

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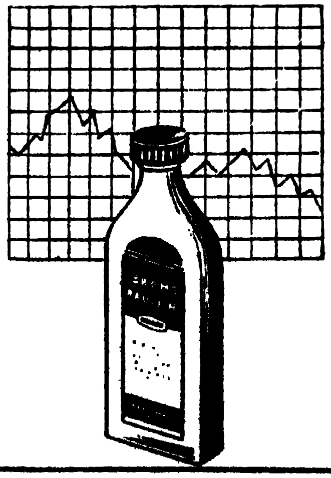

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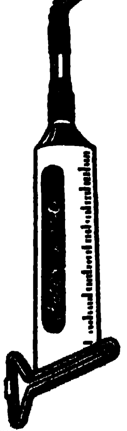

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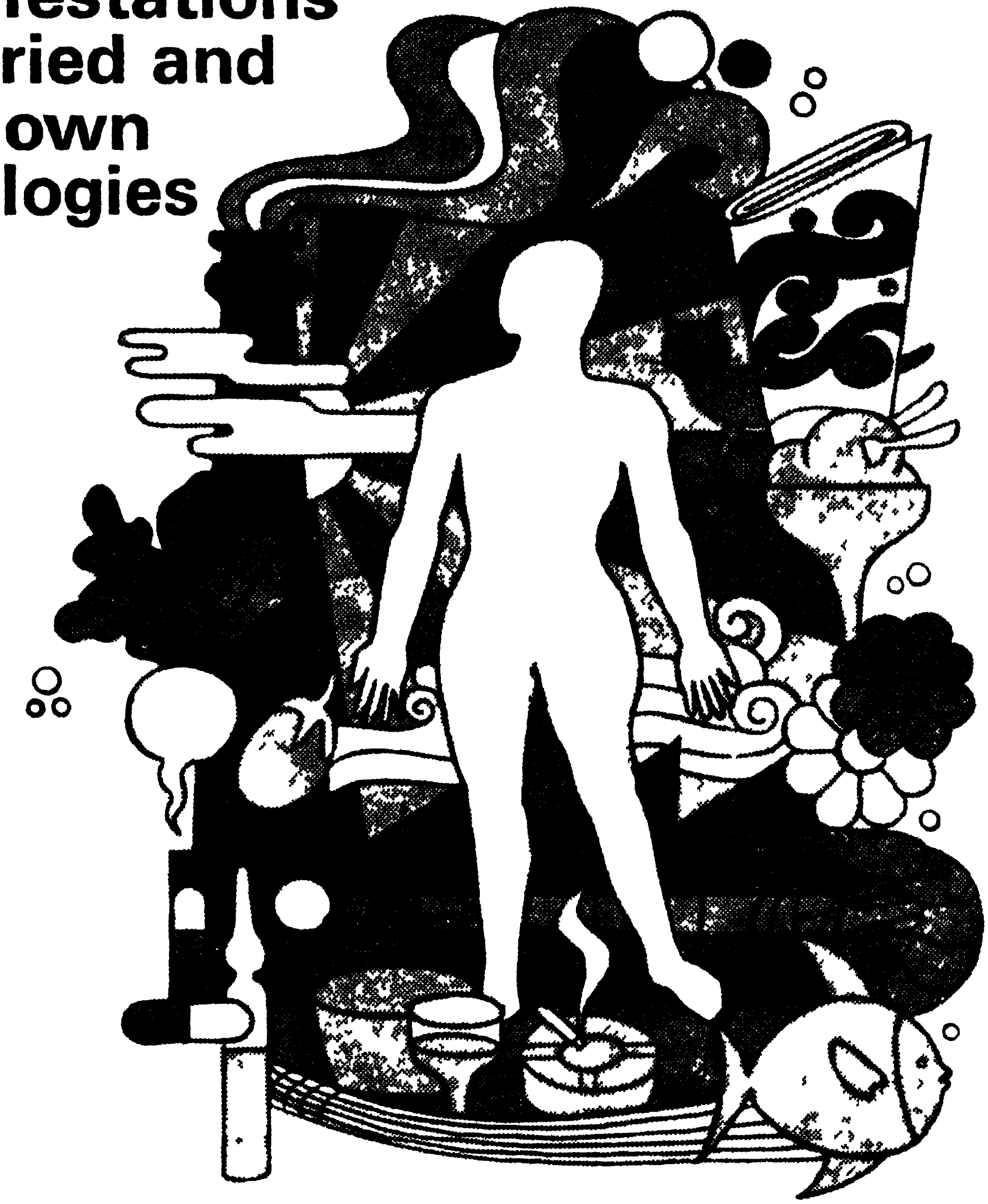

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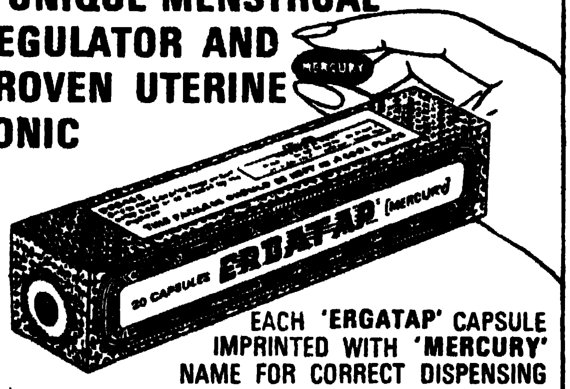

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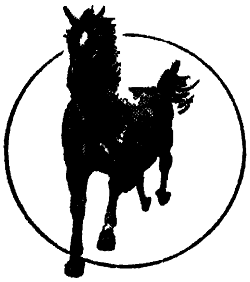

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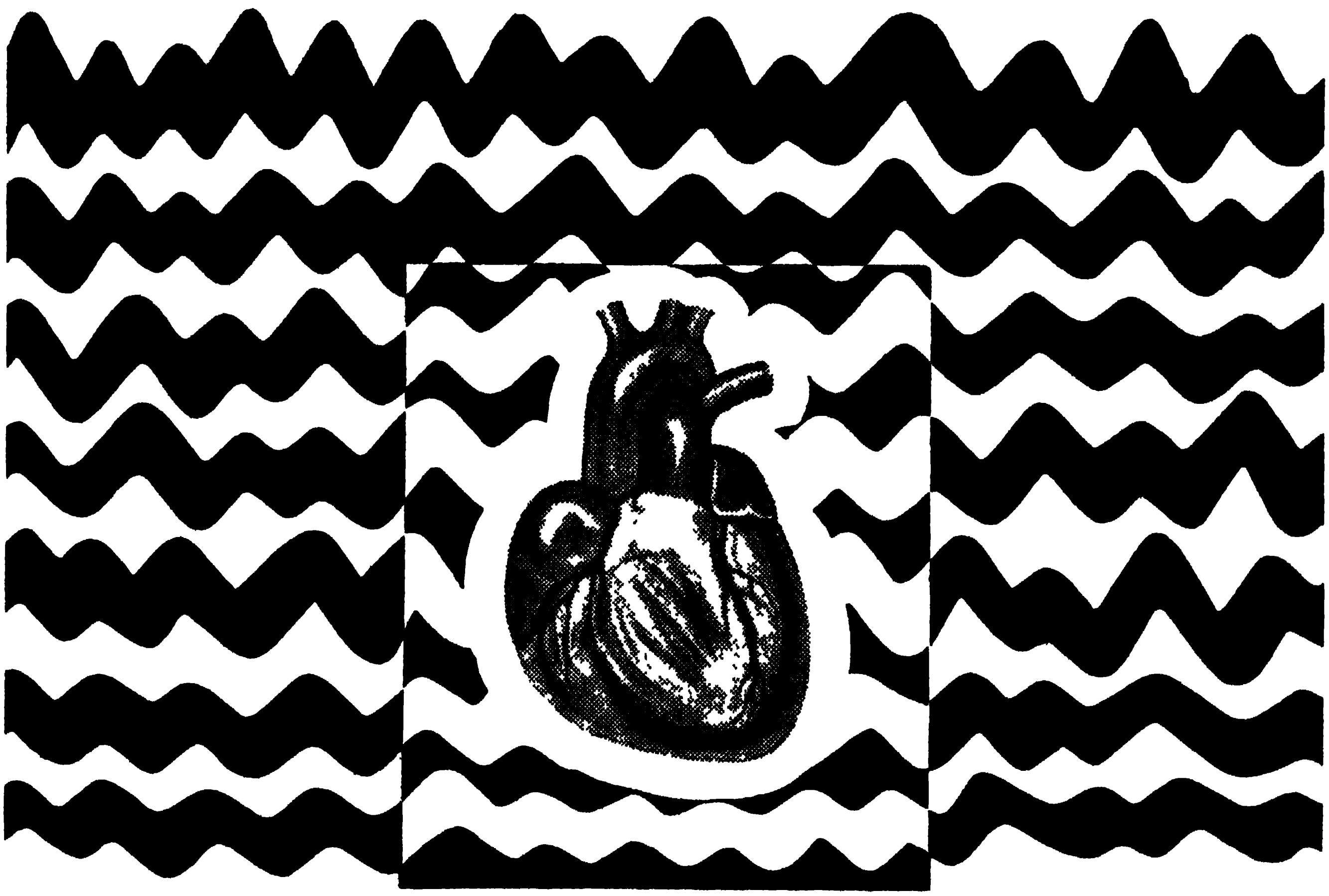

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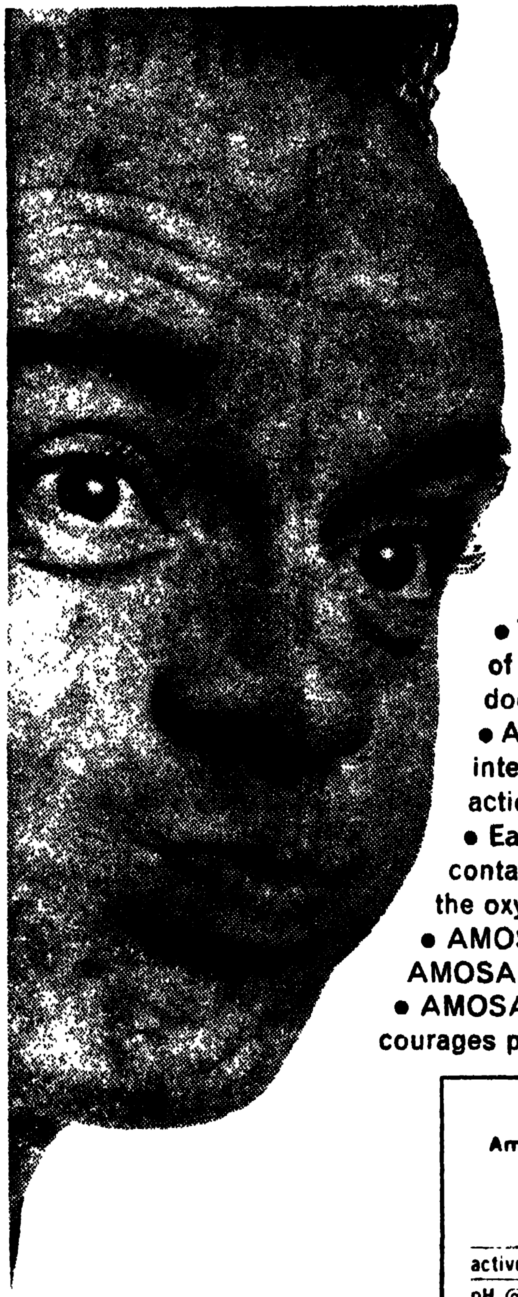

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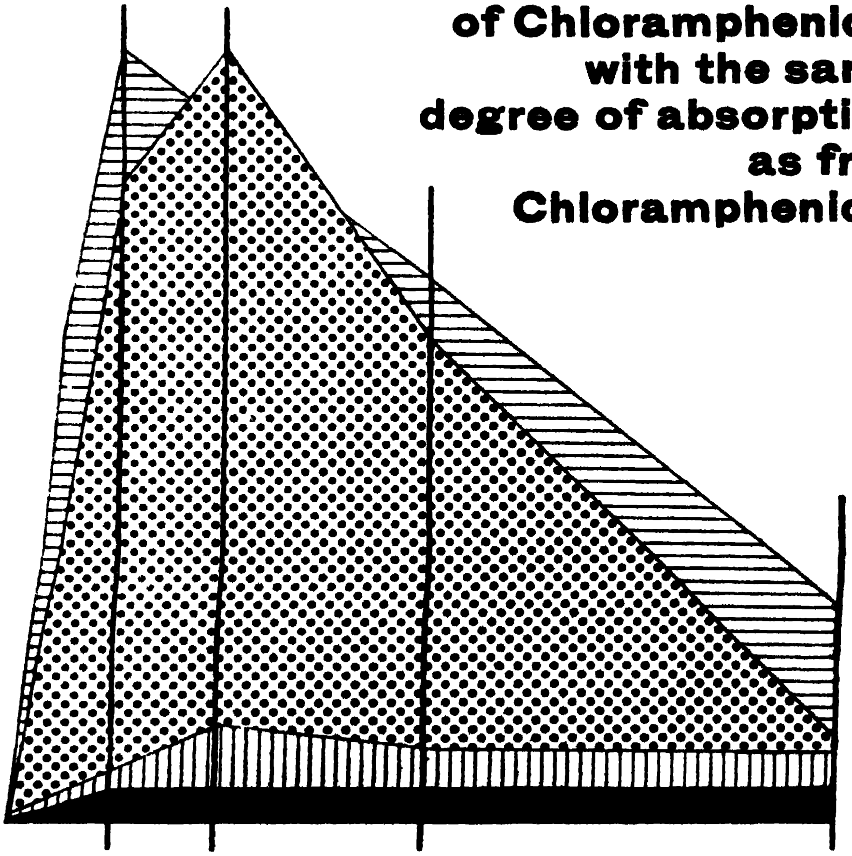

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NUMBER 1 | EDITOR—A. B. MUKERJEE, M.D. (CAL.), F.R.C.P. (LOND.) | JANUARY 1, 1975

ORIGINALS AND PAPERS

1

Non-Specific Stenotic Lesions of Small Bowel

J. D. WIG*, N. K. MONGA**, S. P. KAUSHIK***, H. S. SACHDEVA****

[*Received for publication March 30, 1974*]

There has been a growing awareness in the recent past of small bowel lesions which closely simulate tuberculosis and/or Crohn's disease macroscopically but on detailed examination no histological or microbiological proof of any specific pathology is available (Watson, 1963; Kidd and Vanderpool, 1971). Although majority of ulceroconstrictive lesions of bowel in India are tuberculous (Anand, 1956; Wig *et al.*, 1961), the existence of non-specific ulceration and stricture has recently been reported (Tandon *et al.*, 1966; Prakash *et al.*, 1970). Recognition of this type of lesion in early stages is often difficult. The first signs are usually due to complications, e.g., obstruction, bleeding or perforation and such cases are invariably labelled and treated as tuberculosis.

MATERIAL AND METHOD

The present is a study of 9 cases of non-specific ulceroconstrictive lesions of small bowel treated in one of the surgical units of Postgraduate Institute of Medical Education and Research, Chandigarh, since 1971. During the period under review, tuberculosis and Crohn's disease were found to be responsible for stricture formation in 16 and 8 cases respectively, while malignant stricture was seen in one case only.

OBSERVATIONS

Age and sex—There were 6 male and 3 female patients in the present study. The youngest patient was 18 years old and the oldest 60 years of age. 20-40 years was the most commonly affected age group (60 per cent).

Signs and symptoms—Table 1 shows the presenting features of these cases in order of decreasing frequency. All our cases sought medical advice with intestinal obstruction. Crampy abdominal pain, vomiting and constipation were invariably present. No history of drug intake, pulmonary tuberculosis, coronary insufficiency or thrombo-embolic phenomenon was available in any case. History of subacute or recurrent obstruction was present in 7 cases.

Table 1—*Showing Presenting Features in 9 Cases*

Presenting feature	No. of cases
Crampy abdominal pain	9
Vomiting	9
Abdominal distension	9
Constipation	7
Visible peristalsis	3
Palpable mass	1

The duration of the symptoms varied from 3 days to 6 months.

None of these patients received antituberculosis therapy.

Visible intestinal peristalsis was seen in 5 cases, generalised distension of abdomen was present in 9, and a mass was palpable in 1 case only.

Diagnosis—A pre-operative diagnosis of intestinal obstruction was made on the basis of clini-

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cal history, abdominal signs and preliminary investigations in all the cases. The cause of obstruction was thought to be tuberculosis in 6 cases (66 per cent).

Investigations—Anaemia with haemoglobin level below 10g. per cent was present in 7 patients. Chest x-ray was done as a routine in all cases while pre-operative ESR and mantoux test were done in 3 patients only. None of the pre-operative investigations contributed to any specific pathology. Postoperative chest x-ray, sputum examination and mantoux test were negative in all cases. Plain x-ray abdomen showed multiple fluid levels. Barium studies were not done in any case.

Operative findings—All the cases were subjected to surgery after pre-operative preparation with intravenous fluids and Ryle's tube aspiration. The appearances of the bowel at operation closely mimicked those of tuberculosis or regional enteritis. Tuberculosis was the operative diagnosis in 6, Crohn's disease in 2 and ischaemic enteritis in 1 patient. A solitary stricture in terminal ileum with proximal dilatation was found in each case. Serosal surfaces were markedly hyperaemic in the immediate area of stricture and there was no gross thickening of the wall or mesentery. Regional lymph nodes were soft and enlarged in 3 cases. There was no peritonitis and rest of the gastro-intestinal tract was normal .Marked adhesions were seen in one case who had a previous laparotomy done for traumatic haemoperitoneum one year ago. Excision of the involved segment with normal cuff of bowel on either side with regional lymph nodes was performed in 9 cases.

Pathology—A tight stricture, not admitting even a finger, with proximal ileal dilatation was present in all cases (Fig. 1). On opening the bowel mucosa appeared to be intact over the stricture but ulcerated and haemorrhagic just proximal to it.

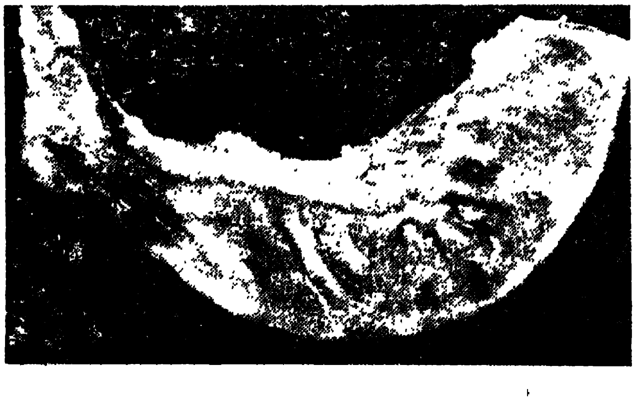

Fig. 1—Showing the Tight Stricture with Proximal Ileal Dilatation

Microscopically, proximal and distal bowel appeared to be normal. At the site of ulceration there was intense lymphoid and plasma cell infiltration with fibrosis of submucosa and muscularis but no granuloma formation (Fig. 2, H. & E.× 50). Full thickness fibrosis was present at the site of stricture. Certain areas showed small vessel thrombi but definite evidence of ischaemic changes was not present except in one case. Lymph nodes showed non-specific inflammatory changes. No organism was seen on acid fast staining.

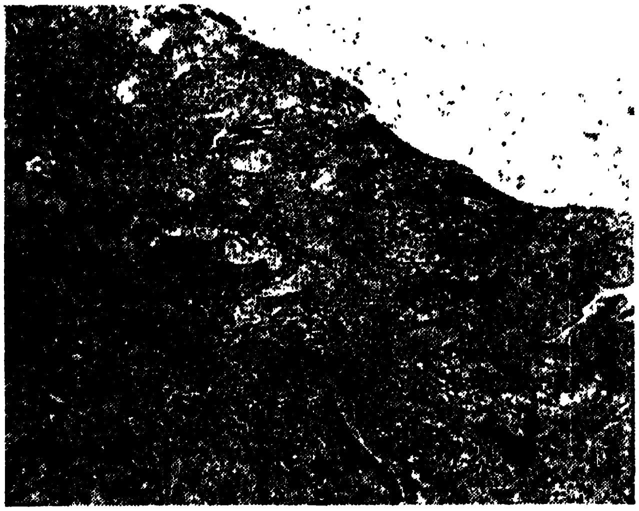

Fig. 2—Showing Intense Lymphoid and Plasma Cell Infiltration at Site of Ulceration

DISCUSSION

Relatively a few published reports have appeared on benign fibrous stenosis of the small bowel. Watson *(loc. cit.)* reviewed the world literature and reported 170 cases of non-specific ulceration and stricture formation to date. Since then, many reports of similar small bowel lesions have appeared in the literature. Tandon *et al.* *(loc. cit.)* reported 12 cases of this kind, and postulated that an altered immune reaction to tuberculous infection may be responsible for the non-specific histological picture, as seen in these cases. Similar lesions have been reported following the use of enteric coated potassium, vascular insufficiency, necrotising arteriolitis, uraemia, coeliac disease, radiation to pelvis and abdomen and drugs like digitalis, chlorpromazine and butazolidine (Sturges and Krone, 1973). Hypersensitivity has also been suggested as a possible factor in their pathogenesis (Rao *et al.*, 1973). None of the factors mentioned above have been confirmed in our cases and the cause remains unknown.

Could it be due to an altered reaction of a few patients to tuberculous infection or the histological picture may have varied because of chemotherapy ? While it may be difficult to rule out such a possibility in our cases, none of the investigations done before or after surgery have proved helpful and to our knowledge none of the cases received specific chemotherapy.

Grossly, the lesions are indistinguishable from tuberculosis and regional enteritis, but they tend to remain single, involve one segment of small intestine, rarely involve regional lymph nodes or mesentery and do not form granulomas (Watson, *loc. cit.*).

In spite of the different aetiological agents, the histological lesion in the bowel remains uniformly the same. Localised vascular injury and thrombosis leads to ischaemia, infarction and ulceration of mucosa (Boley *et al.*, 1965 ; Kidd and Vanderpool, *loc. cit.*). Brisk bleeding may occur if a small artery is eroded in the wall (Korobkin *et al.*, 1971). The base of ulcer is lined by granulation tissue infiltrated with lymphocytes and plasma cells. If perforation does not occur, healing takes place by fibrosis leading to stricture formation and obstruction.

Intestinal obstruction is the commonest mode of presentation. However, a few cases may present with severe haemorrhage (Korobkin *et al. loc. cit.*), or perforation and peritonitis (Shack, 1966).

Segmental resection of the bowel and end to end anastomosis is the treatment of choice and none of the cases in our series have shown any evidence of recurrence so far.

There has been only one death in the present series.

SUMMARY

Nine cases of ulceroconstrictive lesions of the small bowel with no specific aetiology have been presented and the possible factors in their pathogenesis discussed. At laparotomy, it is often difficult to differentiate such lesions from tuberculosis or Crohn's disease and diagnosis is based on microscopic examination, and exclusion of specific disease by various investigative procedures. Treatment is segmental resection of the bowel and is curative in majority of cases. Specific treatment with chemotherapeutic agents is not required. Both the mortality and recurrence rates are low.

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Correlation Study Between Sphygmomanometric and Intraluminal Estimation of Blood Pressure in Hypertensive Subjects

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MALAY SEN GUPTA***

[*Received for publication July 31, 1974*]

The measurement of lateral pressure exerted by the blood column on the arterial wall (blood pressure) has become an integral part of every clinical examination. Riva-Rocci's (1896) brilliant discovery has established sphygmomanometric determination of blood pressure as a standard procedure all over the world. This has completely replaced the intra-arterial measurement of blood pressure as there is "reasonable agreement between direct intra-arterial measurements and those obtained by indirect method" (Hamilton

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et al., 1936). The first comparison of pressure measured by direct methods and the indirect methods was made by Wolf and Bonsdorff (1931). The systolic and diastolic readings came within 5 mm. Hg of the values obtained by direct method in less than half the cases. Hamilton *et al.* *(loc. cit.)* compared the brachial artery pressure measured directly by the optical capsule and indirectly by the auscultatory method. The indirect measurements were on an average 3-4 mm. too low for the systolic and 9 mm. too high for the diastolic, using "fading of the 4th phase" as the criteria for the diastolic pressure. Roberts *et al.* (1953), on the contrary, observed better correlation with respect to diastolic pressure, when sudden diminution in intensity was taken as the measure of diastolic pressure. Kolestsky *et al.* (1965) also made similar observation with respect to diastolic blood pressure.

The indirect measurements of blood pressure are further influenced by the arm size and Ragan and Bordley (1941) observed that with thick arms the record tended to be too high, while with thin arms the record tended to be too low. To avoid this discrepancy Karvonen *et al.* (1964) suggested to use a cuff size of 14 cm. × 40 cm. instead of standard cuff size of 12 cm. × 23 cm. but this was challenged by Simpson *et al.* (1965). They suggested that the best results were obtained when the cuff size was 12 cm. × 35 cm. Finally, applying a correction factor, variable with the arm size (Table 3), to the indirect measurement of blood pressure Pickering *et al.* (1954) observed that under such circumstances the sphygmomanometer gave values well correlated with that obtained by direct method.

It thus makes the point clear that in determination of blood pressure there are several variable factors which influence the indirect measurements and that correlation studies, made so far, included mostly normotensive persons and rarely any hypertensive individual. There is, therefore, ample scope in this respect for investigation in cases of hypertensive individuals, which form a major bulk of patients attending cardiology clinics today. We have attempted here to correlate arterial blood pressure measured by the two methods in hypertensive subjects and to discuss about the clinical implication thereof.

MATERIAL AND METHOD

Altogether 23 patients were studied. Twenty patients had hypertension of various grades and 3 patients had no hypertension clinically. Patients were given a light breakfast at 8 A.M. and the records were made at 10 A.M. Blood pressure in all cases were measured by the same instrument and by the same person. The cuff size of the instrument was 12 cm. × 23 cm. The sphygmomanometric record was made at the left popliteal artery while intra-arterial pressure was measured from the right femoral artery with the help of Statham transducer and with direct writing arrangement on electrocardiogram paper. In auscultatory method, complete disappearance of the sound was used as the criteria of diastolic pressure. The femoral artery was negotiated by Seldinger's (1953) technique under local anaesthesia. No premedication was used in any case. The patients were not receiving any antihypertensive drugs for 5 days prior to investigation. In 12 patients the measurement were recorded at interval of a week and the results were reproducible.

RESULTS

The auscultatory and intra-arterial pressure findings are shown in Table 1.

Table 1—*Showing Auscultatory and Intra-arterial Pressure as Recorded in 23 Patients*

Case No.	Systolic blood pressure (mm. Hg)		Diastolic blood pressure (mm. Hg)	
	Auscultatory	Intra-arterial	Auscultatory	Intra-arterial
1	170	150	122	100
2	210	168	140	112
3	250	264	140	144
4	220	272	110	136
5	260	320	140	184
6	182	172	120	135
7	215	180	110	100
8	240	252	110	125
9	170	200	110	100
10	210	240	100	110
11	180	170	100	110
12	230	260	110	122
13	260	262	115	130
14	260	264	110	125
15	190	172	100	105
16	190	212	115	125
17	220	245	115	130
18	192	200	110	105
19	154	162	100	95
20	260	290	125	150
21	150	184	80	80
22	90	92	70	70
23	100	100	70	70

The relationship between auscultatory and intra-arterial pressure records is shown in Table 2.

From Table 2 it appears that the systolic blood pressure recorded by the conventional sphygmomanometric method differed from that recorded by the direct (intraluminal) method by more than 20 mm. Hg (marked difference) in 12

Table 2—***Showing Relationship Between Auscultatory and Intra-arterial Pressure Recorded in 23 Cases***

Variations in recorded values	Systolic pressure No. of cases (%)	Diastolic pressure No. of cases (%)
A. Sphygmomanometric record higher than intraluminal record:		
a) Higher than 20 mm. Hg	2 (8.7)	2 (8.7)
b) Higher by 10-20 mm. Hg	4 (17.4)	2 (8.7)
B. Sphygmomanometric record lower than intraluminal record:		
a) Lower by more than 20 mm. Hg	10 (43.5)	3 (13)
b) Lower by 10-20 mm. Hg	2 (8.7)	9 (39.1)
C. Sphygmomanometric record within 5-9 mm. Hg of intraluminal record	5 (21.7)	7 (30.4)

subjects ; in 10 subjects (43.5 per cent), the sphygmomanometric record of systolic blood pressure was lower than the direct recording while in 2 subjects (8.7 per cent) the reverse occurred. In 6 subjects the difference in the record of systolic blood pressure by the two methods ranged from 10 mm. Hg to 20 mm. Hg (moderate difference). Of these 6 subjects, sphygmomanometric record was higher in 4 subjects (17.4 per cent) and lower in 2 subjects (8.7 per cent) when compared with the records observed by the direct method. In 5 subjects (21.7 per cent), the record of the systolic pressure measurement by the two methods came within the range of 5-9 mm. Hg (slight difference). As regards diastolic pressure, a difference of more than 20 mm. Hg in the records by the two methods was observed in 5 subjects ; in 2 subjects (8.7 per cent) the sphygmomanometric record was higher than the direct recording while in 3 subjects (13 per cent), the reverse happened. In 11 subjects such difference ranged between 10-20 mm. Hg. Again, of these 11 subjects the sphygmomanometric record was higher in 2 subjects (8.7 per cent) and lower in 9 subjects (39.1 per cent) when compared with the records made by the direct method. In 7 subjects (30.4 per cent), the difference in the record of the diastolic pressure measured by the two methods ranged between 5-9 mm. Hg.

The correction factor for arm circimference as applied to auscultatory recording of blood pressure is shown in Table 3, based on data from Ragan and Bordley (*loc. cit.*) prepared by Pickering *et al. (loc. cit.).*

Table 3—*Showing Correction Factor for Arm Circumference to be Applied to Auscultatory Measurements of Arterial Pressure*

Arm circumference (cm.)	Correction factor for systolic pressure (mm. Hg)	Arm circumference (cm.)	Correction factor for diastolic pressure (mm. Hg)
15-18	Add 15	15-20	No correction
19-22	Add 10		
23-26	Add 5	21-26	Subtract 5
27-30	No correction	27-31	Subtract 10
31-34	Subtract 5	32-37	Subtract 15
35-38	Subtract 10		
39-41	Subtract 15		
42-45	Subtract 20	38-43	Subtract 20
46-47	Subtract 25	44-47	Subtract 25

The correlation between auscultatory method and intraluminal pressure records is shown in Table 4, applying correction factor of Pickering *et al. (loc. cit.).*

Table 4—*Showing the Incidence of Correlation Between Auscultatory and Direct Intra-arterial (Intraluminal) Blood Pressure Record*

Variation in recorded values	Systolic pressure No. of cases (%)	Diastolic pressure No. of cases (%)
A. Sphygmomanometric record higher than intraluminal record:		
a) Higher than 20 mm. Hg	4 (17.4)	2 (8.7)
b) Higher by 10-20 mm. Hg	1 (4.35)	—
B. Sphygmomanometric record lesser than intraluminal record:		
a) Less by 20 mm. Hg or more	8 (34.8)	9 (39.1)
b) Less by 10-20 mm. Hg	2 (8.7)	4 (17.4)
C. Sphygmomanometric record within 5-9 mm. Hg of intraluminal record	8 (34.8)	8 (34.8)

From Table 4 it appears that after applying 'correction factor' of Pickering *et al. (loc. cit.)* a marked difference (difference of more than 20 mm. Hg) in the record of systolic and diastolic pressure by the two methods was observed in 12 subjects and 11 subjects respectively ; the sphygmomanometric record of systolic and diastolic pressure was higher than the direct recording in 4 subjects (17.4 per cent) and 2 subjects (8.7 per cent) respectively while the former record was lower than the latter record in 8 subjects (34.8 per cent) and 9 subjects (39.1 per cent) respectively. A moderate difference of 10-20 mm. Hg in the record of systolic and diastolic pressure by the two methods was observed in 3 subjects and 4 subjects respectively. The sphygmomanometric record of systolic pressure was higher than the record obtained by the direct method in 1 subject (4.35 per cent) and lower in 2 subjects (8.7 per cent) ; and in the case of diastolic pressure the sphygmomanometric record was lower than the direct recording in 4 subjects (17.4 per cent). The systolic and diastolic pressure recorded by the two methods came within the range of 5-9 mm. Hg in 8 subjects (34.8 per cent) in each.

DISCUSSION

The present study shows that good correlation (difference of record by the two methods less than 10 mm. Hg) was obtained in about 22 per cent cases with respect to systolic and 30 per cent cases with respect to diastolic blood pressure (Table 2). Incidence of poor correlation (difference more than 20 mm. Hg) was found in about 52 per cent of cases with respect to systolic pressure and in about 22 per cent cases with respect to diastolic pressure. The maximum difference between the systolic and diastolic blood pressure in two methods were 60 mm. Hg and 44 mm. Hg respectively (case 5). Repetition of the procedure did not show any significant alteration in 12 cases. No complication occurred in any case due to the procedure.

After applying correction factor of Pickering *et al. (loc. cit.)*, the incidence of good correlation improved to about 35 per cent of cases (Table 4). The incidence of poor correlation (difference more than 20 mm. Hg), however, was found in 52 per cent cases in respect of systolic and about 48 per cent cases in respect of diastolic blood pressure. The maximum difference between systolic and diastolic blood pressure in two methods were reduced to 55 mm. Hg and 39 mm. Hg respectively. The three control cases showed good correlation as regards diastolic pressure but in one case the systolic pressure observed by sphygmomanometer was too low as compared to that obtained by direct method.

SUMMARY AND CONCLUSION

Altogether 23 patients were studied of which 20 patients were hypertensive and 3 patients had normal blood pressure. Direct and indirect measurements of blood pressures were made in all cases. In 12 patients measurements were repeated after an interval of a week.

Overall correlation between indirect and direct measurement of blood pressure is poor in hypertension cases. Hence, in hypertensive persons, unlike the normotensives, one should not always rely only on the sphygmomanometric record. Sphygmomanometric method may show either higher or lower arterial blood pressure than the actual blood pressure in the hypertensive persons and consequently hypotensive therapy in such persons may show erratic response.

ACKNOWLEDGMENT

Our thanks to Surgeon Commodore, Dr. G. C. Mukherjee, Principal-Superintendent, Nilratan Sircar Medical College and Hospital for kindly permitting us to utilise the hospital records and to Dr. Samir Roy, for his active help in carrying out the investigations.

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PRACTITIONERS' SERIES

Stapedectomy

P. N. AGARWAL*

Stapedectomy, as a means to provide immediate as well as long lasting hearing improvement in deafness from otosclerosis or other causes of stapedial footplate fixation, has become a standard surgical procedure. With better diagnostic and operative facilities and prospects of excellent postoperative results, this operation is being performed more commonly. However,

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an unexpected operative findings, either of advanced degree of disease or of other associated lesions, may prove to be demanding on the skill of the operator and requires familiarity on his part with various techniques of the operation. Following is an account of five such unusual cases.

ILLUSTRATIVE CASES

PANOSSICULAR FIXATION:

S.B., 35 years, female, was seen on 12-5-1969 with complaints of deafness and tinnitus in right ear for last one year. Nothing relevant in past history or family history could be obtained.

Examination revealed intact but slightly thickened pars tensa and a shallow invagination pouch of Shrapnell's membrane in right ear. No abnormality was detected in left ear. Valsalva manoeuvre was positive in both ears. Weber test lateralised to right ear, with negative Rinne in right ear and positive in left ear.

Audiogram showed normal threshold of hearing with bone conduction, but increased threshold of hearing with air conduction—denoting pure conductive deafness.

Management—Right ear was explored under local anaesthesia on 14-5-1969. Shrapnell's membrane was adherent to neck of malleus. Incudostapedial joint had complete bony ankylosis. Tendon of stapedius—NAD. Footplate of stapes was uniformly thickened and fixed completely. Owing to extreme limitation in mobility of long process of the incus, the malleo-incudal joint was explored which was seen to have undergone changes similar to that of incudostapedial joint. The ossicular mass in attic was fixed to attic walls. Round window and mucosa of middle ear revealed no abnormality, superstructure of stapes fractured away from fixed footplate. Long process of incus was cut at its junction with body of incus and removed along with attached superstructure of stapes. Malleus was decapitated and in the process of removing malleo-incudal joint, head of malleus got separated and was removed. Body of incus could not be removed owing to firmer fixation. Footplate was removed in pieces. Fat and wire prosthesis, with pars tensa was brought in contact with loop of wire. The patient had mild vertigo and vomiting with nystagmus to right side of 1st and 2nd degree in the postoperative period. This cleared off within 4-5 days. There was satisfactory improvement in hearing but there was no change in tinnitus.

Postoperative audiogram on 3-6-1969 showed elevation of air conduction curve to normal limits and marked reduction of the gap between air conduction and bone conduction curves.

Comments—Panossicular fixation along with bony ankylosis of interossicular joints is rarely seen. In the present case, with the absence of a history of trauma or of past suppuration and with the absence of any evidence of generalised bony or articular disease, most probably the fixation was brought about by post-catarrhal fibro-osseous changes. This possibility is supported by the findings of thickened pars tensa and invagination and adhesion of pars flaccida. The causes of individual or multiple ossicular fixation include otosclerosis, congenital, post-traumatic, post-inflammatory tympanosclerosis, fixed malleus head, calcification of intratympanic muscle tendons and some other conditions like rheumatoid disease, Paget's disease, van der Hoeve-de Kleyn syndrome, osteitis fibrosa cystica and fibro-osseous dysplasias.

This case not only emphasises the importance of routine palpation for mobility of malleus and incus in cases undergoing stapedectomy, but also calls for the preparedness of the surgeon to use bone cutting instruments in this operation as well as his familiarity with the steel wire technique; as in these cases an incus replacement prosthesis or a prosthesis, as described herein has to be used.

ABSENT STAPEDIUS TENDON:

H.S., 60 years, male, was seen on 3-7-1973 with deafness and low pitched tinnitus in both ears for last 5 years.

Examination of ear, nose and throat was normal except for bilateral mixed deafness, predominantly of the conductive type.

Audiogram: Bone conduction curve showed loss of hearing for higher frequencies while air conduction showed loss of hearing for all frequencies, more marked for higher frequencies.

Management—Right ear was explored under local anaesthesia on 10-7-1973. There was complete absence of stapedius tendon: Footplate was irregularly thickened and completely fixed. Stapedectomy was done and fat wire prosthesis was given. No other middle ear abnormality was seen.

Postoperative audiogram was done on 25-7-1973 which showed complete improvement of conductive component of hearing loss, the sensorineural component of hearing loss resisted, as expected.

Comments—Whether this absence of stapedius tendon was congenital or as a result of some atrophic process is difficult to determine. However, associated absence of pyramidal eminence and of any attachment sign to neck of stapes makes it more likely to be congenital. There was no history of any trauma or of previous operation or of any other ear trouble.

Absence of stapedius tendon does not modify in any way the operation or its postoperative period as it is almost routinely cut in this operation, when present. Whether the high frequency sensorineural loss was due to presbycousis or as a result of increased possibility of acoustic trauma difficult to analyse. However, in this case, whereas the absence of stapedius exposed the cochlea more to acoustic trauma, the associated presence of stapedial fixation helped in safeguarding against this.

Congenital absence of stapedius is seen in 8 out of 1000 middle ear operations and is present at birth. Middle ear anomalies include absence of stapedius muscle and tendon and absence of pyramidal eminence (Sando and Wood, 1971).

NARROW OVAL WINDOW NICHE:

G.K.C., 20 years, male, was seen on 13-10-1971 with progressive deafness in right ear for last 1 year, high pitched tinnitus in right ear for 6 months and vague vertiginous feeling for 6 months. ENT examination revealed positive Schwartze's sign in both ears—more marked in right ear. Negative Rinne both ears, with Weber lateralised to right ear. Caloric tests were normal in both ears, conversational voice could be heard in right ear up to 7 feet and up to 15 feet in left ear. Speech discrimination improved with amplification.

Management—Right ear was explored under local anaesthesia on 20-10-1971. The footplate was uniformly thickened and completely fixed all round and was covered with very marked overhang of deposits of new bone covering the promontory and portion of fallopian canal adjacent to the oval window, thereby reducing the oval window area to a narrow and deep gutter. A hand trephine was used to complete stapedectomy and a fat-wire prosthesis given. Round window was normal. Postoperative recovery was uneventful and the patient could hear conversational voice in right ear up to more than 20 feet with a positive Rinne when last seen on 11-11-1972.

Comments—The operative findings of heaped up bone over the promontory and portion of fallopian canal, adjacent to oval window, on the one hand, explains the clinical features of high pitched tinnitus and vertiginous feeling along with a positive Schwartze's sign but on the other hand makes the operation more difficult by compromising the operative field. The heaped mass of bone was not disturbed for fear of inducing bleeding from the actively diseased area. A steel wire prosthesis seems to be ideal for these oval windows situated at the bottom of a deep and narrow gutter.

The Schwartze's sign is seen in about 2 per cent of new cases, usually young adults with widespread active disease and it carries a poor prognosis (Morrison, 1971). Ruedi (1969) demonstrated venous shunts between vessels of otosclerotic lesion involving promontory and capillaries of overlying mucosa. This produces vascular swelling of mucosa seen as Schwartze's sign. Similar shunts have been described by him between vessels of otosclertoic lesions and membranous labyrinth blood supply. This case has so far kept up his improvement in hearing, is free from vertigo and his tinnitus is somewhat less than what it was before the operation. Nevertheless, Schwartze's sign serves to forewarn the surgeon for careful preoperative cochlear function tests, for his preparedness for possible operative difficulties and for careful postoperative follow-up. It may be wise to postpone the other ear surgery till this sign fades out either spontaneously or as a result of drugs like sodium fluoride.

THE PERILYMPH GUSHER:

P.C., 20 years, male, was seen on 20-1-1971 with deafness and tinnitus in both ears for last 3 years. There was no vertigo.

Examination revealed intact drums, patent eustachian tubes and bilateral conductive deafness.

Audiogram on 1-2-1971 showed severe loss of hearing in all frequencies by air conduction.

Management—Left ear was explored under local anaesthesia on 2-2-1971. The footplate was uniformly thickened like a biscuit and completely fixed. A hand trephine was used to drill a hole in the footplate and this was 'greeted' by a persistent and profuse gush of perilymph, filling in no time the whole middle ear and then the external canal, ear speculum and finally overflowing to the edges of the speculum. The gush did not show any sign of subsiding even after waiting a few minutes and further raising the head end of table. Using continuous suction it was possible to complete the operation and a fat-wire prosthesis given. This stopped the gush completely. No other middle ear abnormality was seen. The external meatus was packed and compression bandage given. The patient had slight perilymph leak for three days postoperatively, necessitating frequent changing of wet bandage. He was given diuretics and 50 per cent glucose I.V. in the postoperative period and the ear was completely dry on the 4th postoperative day. No other problem was encountered in the postoperative period. There was satisfactory hearing improvement.

Postoperative audiogram on 30-3-1972 showed good improvement in hearing in all frequencies by air conduction.

Comments—The perilymph gushers, though extremely rare, are more commonly expected and encountered with congenital stapes fixation than with otosclerosis. In the later condition, it might happen once in 500 stapedectomies (Morrison, *loc. cit.*). The gushing may arise from an overtly patent cochlear aqueduct or from perineural pathways of the internal auditory canal. Yet, another interesting condition where these gushers might be encountered is perilabyrinthine hydrops—usually presenting as fluctuating mixed deafness in congenital deaf children (Farrior and Endicott, 1971). The present case does not fit with congenital stapes fixation in view of historical duration of deafness, absolutely normal speech development in spite of bilateral deafness of approxi-

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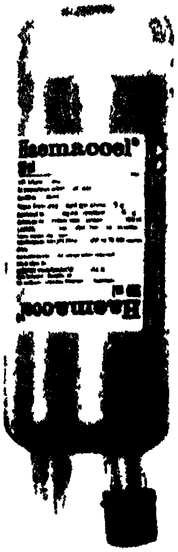

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mately 60 Db. for the speech frequencies and absence of any schooling handicap. Perilabyrinthine hydrops is again not likely in view of the absence of any fluctuations in hearing loss and of any inner ear symptoms. In perilabyrinthine hydrops, the perceptive deafness component has been ascribed to compression of endolymphatic system and conductive deafness component to jamming up of footplate against overhanging anterior lip of oval window (Farrior and Endicott, *loc. cit.*). The finding of fixed and thickened footplate in the present case is not in favour of perilabyrinthine hydrops.

When confronted, complete and permanent stoppage of the gush is imperative. The fat of the fat-wire prosthesis serves as a "soft cork" to close effectively the mouth of the "bottle" and the steel wire connection to incus counteracts any tendency for the "cork" to come out. Of course, if the perilymphatic pressures are too high, this technique may not succeed and then recourse may have to be taken to other methods viz, packing the middle ear and meatus followed by treatment to reduce perilymphatic pressures and operating again after a few days or weeks; ablation of cochlear aqueduct through an anterior or a posterior approach (Farrior and Endicott, *loc. cit.*); perineural grafting of internal auditory meatus and obliterative procedures of middle ear by tissue (Paparella, 1971), whether drainage of CSF by a lumbar puncture will be safe and helpful in reducing the perilymph gush and thereby completing the operation is conjectural.

These cases require careful vigilance in the postoperative period particularly for any features of perilymph fistula or a frank perilymph otorrhoea or otorhinorrhoea.

COMBINED ROUND WINDOW AND COCHLEAR OTOSCLEROSIS:

N.D.K., 30 years, male, was seen on 1-5-1973 with deafness in both ears for 19 years, tinnitus—occasional and high pitched in both ears—19 years. No history of vertigo. A positive family history of deafness was present. The patients' voice was unmistakably soft and quiet.

Examination revealed considerable concentric narrowing of lumen of left bony external meatus; both drums were intact with eustachian tubes patent. There was no Schwartze's sign in either ears. Weber was lateralised to left ear. Rinne—positive in right ear and negative in left ear with reduced absolute bone conduction in both ears. Conversational voice could be heard up to 3 feet only in right ear and was nil in left ear. However, his speech discrimination improved with intensity amplification in both ears.

Pre-operative audiogram on 8-5-1973 showed loss of hearing in all frequencies but the loss was more with air curve than with bone curve—mixed type of deafness.

Management—The left ear was explored under general anaesthesia. In view of narrowing of meatus, a postaural approach was used. After elevating skin from the bony meatus, its lumen was widened by electric burr. The mastoid was found to be sclerosed. Tympanotomy revealed an intact ossicular chain with mobile footplate. The incudostapedial joint was jammed against the hyperostosed bone from posterior wall of middle ear. This bone was drilled away to allow free movement of this joint. Round window (RW) niche was completely obliterated by bone. Mucosa of middle ear was diffusely thickened and mildly oedematous. A hand burr was used to remove bone from RW area—following which perilymph was seen through the hole made and this gave a normal RW reflex response. A tiny plug of fat used to cover the hole over which mucosa of middle ear was reflected back. In the postoperative period, he had mild vertigo lasting for 3-4 days with nystagmus of 1st degree to left side. This subsided with usual antivertiginous drugs. Hearing tests were repeated on 23-7-1973. Weber was lateralised to left ear with Rinne negative in left ear and positive in right ear with reduced absolute bone conduction in both ears. Conversational voice 3 feet in right ear and nil in left ear, speech discrimination improved with amplification of both ears.

Postoperative audiogram showed no significant change than pre-operative readings.

Comments—This case presents a rare combination of a number of pathological changes viz., hyperostosis of bony meatus and posterior tympanic wall, a jammed incudostapedial joint against bony outgrowth, osseous closure of RW niche, thickened mucosa of middle ear and inner ear changes suggestive of cochlear otosclerosis. At the present stage of our knowledge it is difficult to attribute all these changes to one common entity i.e, otosclerosis. With a history of childhood operations on tonsils and adenoids and submucus resection operation, perhaps thickened mucosa of middle ear could be explained on the basis of chronic catarrhal changes. It is interesting to observe the presence of high pitched tinnitus in this case as well as case 3 who also showed excessive exostosis, in his case, of oval window area. In this light, case 3 requires a follow-up over a number of years for any development of cochlear otosclerosis. Ruedi (*loc. cit.*) demonstrated abnormal venous channels between an active otosclerotic focus of cochlear capsule and the blood supply of organ of Corti. These shunts presumably impair the nutrition and oxygenation of sensory epithelium and nerve endings.

With the patient's typical changes of quality of voice, a negative Rinne and a positive speech amplification test along with positive family history and audiometric findings of air bone gap it was fully justified to explore the middle ear in view of the air bone gap, signifying greater loss of air conduction than that of bone conduction. Morrison (*loc. cit.*) cites one example of a case of subtotal deafness due to combined stapedial and cochlear otosclerosis with no recordable bone conduction on audiometry but with a Rinne negative with 256 fork—signifying a functioning inner ear. After stapedectomy, there was hearing improvement demonstrating a surprising amount of cochlear reserve. However, in the present case, after freeing the jammed incudostapedial joint, whether it was wise to attempt to create a mobile RW, is debatable. House (1969) says, "Our experience in dealing with otosclerotic closure of RW indicates that if this phenomenon is uncovered, drilling out the RW is contraindicated". Dawes and Curry (1969) however, report, "M.L. is an interesting case for not only had she an extensive focus in the oval window but also in the round window. Drill-out of round window was performed and a perilymph leak developed. This leak was immediately sealed by amnion. The audiogram shows great improvement 5 years later". This case did not have any deterioration in hearing after this procedure. The postoperative persistence of conductive component of his hearing loss is difficult to explain but may be due to inner ear conductive loss as described by House (*loc cit*). Sodium fluoride therapy may not only arrest any further deterioration in hearing loss but also may improve the hearing as described by Shambaugh (1969), citing a case record of combined cochlear and stapedial otosclerosis who had deterioration of hearing following initial improvement from stapedectomy This case improved in his hearing again after sodium fluoride therapy.

SUMMARY

Five unusual cases—one each of panossicular fixation with bony ankylosis of inter-ossicular joints, absent stapedius tendon, narrow oval window niche, perilymphatic gusher and combined round window and cochlear otosclerosis—have been presented and the associated problems briefly discussed.

ACKNOWLEDGMENT

I take this opportunity to thank Mr. W. M. S Ironside, Consultant Otolaryngologist, Huddersfield and Halifax Group of Hospitals, Yorkshire, England, under whose able guidance I learnt the techniques of reconstructive middle ear surgery.

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CASE NOTES

1

Osteopetrosis†

D. SENGUPTA*, M. MITRA**

It is a very rare disease manifested clinically by tendency to fracture, often associated with optic atrophy, anaemia and hepatosplenomegaly, pathologically by brittle bones and radiologically by absence of medullary cavity with alternate dense and light zones. Recently 2 such cases have been reported in Indian literature (Bhattacharya *et al.*, 1963. Menon *et al.*, 1973).

CASE REPORT

A 16-year-old Hindu girl was admitted at the haematological unit with complaints of early fatiguability, stunted growth and a lump in the left side of the abdomen. Repeated failure in performing sternal puncture (as evidenced by broken needles) during routine investigation suggested something abnormal in the bone and accordingly the patient was advised x-ray of all bones when the diagnosis was obvious. Later on, she was referred to our unit for splenectomy as there was evidence of hypersplenism.

Examination—Examination revealed a short statured, pale looking emaciated girl with absence of secondary sexual characters. Liver was 3 fingers and spleen 10 fingers palpable below the costal margin and there was enlargement of parietal prominence. Neurological examination including cranial nerves revealed no abnormality. There was no abnormality regarding vision, no nystagmus and no ocular palsies

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†Paper presented at the Conference of the Association of Surgeons of India (Calcutta Chapter) held on 29th May, 1973.

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**M.S. (Cal.), Clinical Tutor

were detected. Cardiovascular, respiratory and gastro-intestinal systems were normal.

No history of consanguineous marriage in the family was present. Investigation in the form of skiagram only was performed in the living members of the family. The family consisted of 10 members including parents, of which the father died at old age and 6th issue died in infancy. Evidence of osteopetrosis was noted in 1st, 2nd, 7th and 8th issue (the patient)—all of them were sisters. The sisters were all married except the patient (last issue) and they gave birth to children who were examined radiologically but did not reveal any evidence of osteopetrosis.

Investigations—Haemoglobin 54 per cent; plenty of premature RBC in the form of normoblasts, reticulocytes (10 per cent); WBC—4,900/c.mm. with polymorphs—55 per cent, lymphocytes—40 per cent, eosinophils—3 per cent, monocytes—2 per cent; platelets—1.5 lacs; PCV—23 per cent. Serum calcium, phosphorus, alkaline phosphatase, albumin: globulin ratio, urea and NPN were within normal limits.

X-ray showed dense, opaque, structureless osseous system specially in pelvis and vertebral bodies (Fig. 1), base of skull, upper third of femur and lower half of radius and ulna (Fig. 2) obliterating the marrow cavity with expanded ends of long bones and multiple alternate transverse striations. Liver biopsy showed periportal fibrosis with no evidence of haemopoiesis. Splenic puncture showed many lymphocytes, few myelocytes, normoblasts and megakaryocytes. Diminished life span of RBC, determined by Cr 51 study before operation was recorded. Biopsy of spleen showed evidence of erythropoiesis and bone biopsy revealed the typical feature of osteopetrosis.

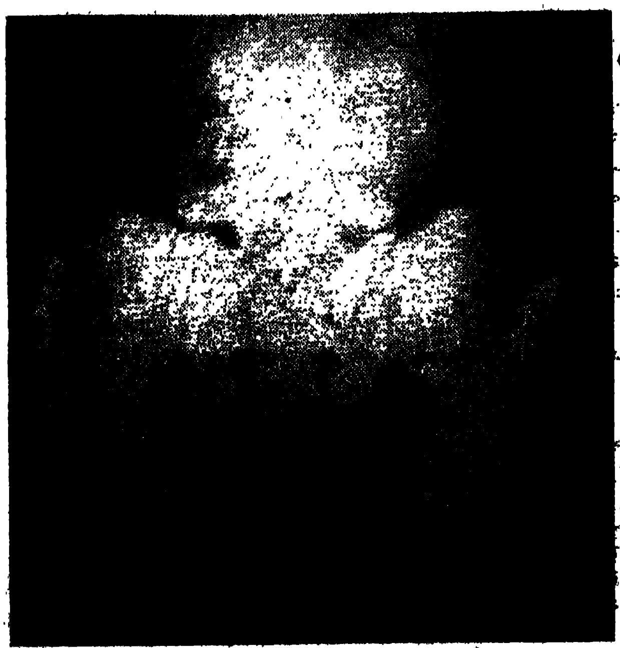

Fig. 1—Showing X-ray of Pelvis and Vertebral Bodies with Dense Opaque Structureless Osseous System

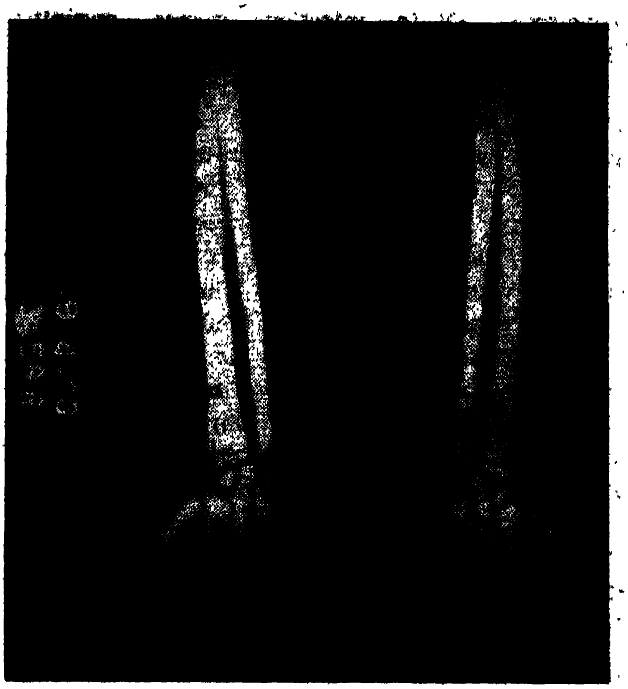

Fig. 2—Showing X-ray of Lower Half of Radius and Ulna with Expanded Ends and Multiple Alternate Transverse Striations

DISCUSSION

Osteopetrosis is a disease characterised essentially by increased thickness and density of the cortical and spongy portion of the entire osseous system. These changes are characteristically, not invariably, associated with myelophthisic anaemia which is not entirely due to the defective erythropoiesis alone but an extracorpuscular haemolytic element has been detected (Menon *et al.*, *loc. cit.*). There may be other manifestations such as multiple pathological fractures, hydrocephalus, optic atrophy and enlargement of liver and spleen. Narrowing of the cranial foramina causes compression of the nerves leading to progressive blindness. Transmission is not sex linked and both sexes are equally affected. But here only female members were affected.

The fully developed syndrome may not be easily diagnosed. All cases, however, do not show the complete complex of symptoms described and may lead to confusion in diagnosis. The possibility of error is greater when only a limited portion of the skeleton is examined radiologically. There are various sclerosing diseases of bone most of which show localisation to a limited portion of the skeleton. This fact emphasises the importance of complete examination of the skeleton when studying a difficult case. In addition to the benign lesion, x-ray appearance of cancerous metastasis in bone is quite different from that of osteopetrosis. Of the infectious process, congenital syphilis frequently produces destruction of bone. Chronic poisoning with lead and phosphorus are known to give rise to dense bands across the metaphysis of growing bones. In such cases, a carefully taken history helps to prevent confusion. Pathologic fracture may ensue from a number of causes of which the condition commonly seen is osteogenesis imperfecta, where the density of bone is decreased rather than exaggerated. There should be little confusion with respect to Paget's disease.

Two different varieties have been described: (a) Infantile malignant form and (b) chronic benign form. Disease may start in utero and early in infancy. Prognosis is very poor in this group. Those whose symptom has been solely pathological fracture and in whom the disease has been discovered incidentally by x-ray examination seem to have very good prognosis (Menon *et. al.*, *loc. cit.*). The patient usually die of progressive anaemia or intercurrent infection. Corticosteroids improve the blood picture and are helpful in the treatment of anaemia. Blood transfusion may be given if necessary. Splenectomy may be considered in case of hypersplenism. In our case, anaemia was corrected following splenectomy.

CONCLUSION

The ultimate cause is unknown but several thought-provoking suggestions have been published in the literature such as role of calcitonin and inorganic pyrophosphate in calcium metabolism (Menon *et al.*, *loc. cit.*). Though no definite treatment can be offered to the patient's suffering, still they will always create enough of academic interest at all times.

ACKNOWLEDGMENT

We are indebted to Dr. B. Chakravarty, Principal-Superintendent and Dr. R. B. Chatterjee, Professor-Director, Department of Surgery, Medical College and Hospitals for permission to carry out this work. We are also thankful to Professor R. N. Roy who has kindly referred this case to us and Shri A. Bose for helping in the isotope studies. We appreciate the excellent technical assistance of Drs. P. K. Roy, P. Sinha, A. Roychowdhury, S. Hazra and S. Chatterjee.

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2

Leriche's Syndrome

RAMAVATAR SHARMA*, B. BHARADWAJ**
C. S. BABEL***

Aortic thrombosis (Leriche's syndrome) is generally considered to be a rare condition. According to Burt *et al.* (1952) the first report of aortic thrombosis appears to have been that by Severinus in 1632. In 1935 Rothstein was able to collect 123 cases from the literature. Leriche in 1932 described in males, a syndrome which consisted of intermittent claudication affecting the gluteal and thigh regions and impotence due to thrombotic obliteration of the aortic bifurcation. In 1948 Leriche and Morel published their experiences with such cases and pointed out that the outlook for these patients was by no means hopeless.

The degree of occlusion process varies from minimal stenosis to complete occlusion. The disease either affects the aortic bifurcation only or is a part of a generalised process affecting the proximal or distal arterial tree. In addition to above, the patient might present with rest pain or even gangrene. Palpation usually shows absent or reduced femoral pulsation. A harsh bruit is usually heard in the femoral region when occlusion is partial. Diagnosis is confirmed by aortography. Price and Wagner (1947) are credited with being the first to have used aortography to demonstrate thrombosis of the abdominal aorta but Leriche in his original paper already refers to cases in which aortography was performed in his clinic before 1942. Since 1947 the method has been used increasingly.

The recorded complications following aortography are paraplegia, pneumothorax, perforation of the bowel, peritoneal injection of the dye, haemothorax and renal failure. About 12 deaths from anuria and renal failure following aortography are recorded in the literature up to 1958. However, Starer and Sutton (1958) stressed that adequate diagnostic results can be obtained using only 15-20 ml. of 60 per cent urografin without any real danger of renal damage. This paper records a case of Leriche's syndrome who died of renal failure after aortography though only 20 ml. of the contrast media was used for that purpose.

CASE REPORT

Sayeed Abu Tayab, 55 years, Mohammedan, male, was admitted in this hospital on 7-5-1973. His com-

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plaints were increasing intermittent claudication in right gluteal and calf muscles for last 6 months; colicky pain around umbilicus, gradual diminution of appetite and nausea for last 4 months. He was a non-vegetarian and used to smoke about 10-15 *biris* per day for last 30 years.

On examination, he was of sthenic built; radial pulse—80/minute, regular in rate, rhythm and volume; BP—140/90 mm. Hg; temperature 37°C; respiration—20/minute; right femoral pulse was feeble while right popliteal, posterior tibial and dorsalis pedis pulsations were absent. The pulsations on the left side in the lower extremity were palpable. The circumference of right calf muscle was about 1.5 cm. less than that of left side. Tenderness around the umbilicus was present.

Investigations—Laboratory investigations revealed total leucocyte count—7,900/c.mm. with polymorphs 64 per cent, lymphocytes 33 per cent, monocytes 1 per cent, eosinophils 2 per cent. Haemoglobin 13 g. per cent, ESR—58 mm. 1st hour, blood cholesterol—138.8 mg. per cent, serum bilirubin—0.5 mg. per cent, blood sugar—66.7 mg. per cent, VDRL—negative; blood urea on 7-5-1973 was 142.8 mg. per cent with trace of albumin in urine without any microscopic findings. Urine culture was sterile.

Management—The patient was treated with I.V. glucose 25 per cent 200 ml. twice daily, crystalline insulin—10 units twice daily, injection of xantinol nicotinate, tablet methandienone and crystalline penicillin. After one week of treatment blood urea which was 142.8 mg. per cent came down to 35 mg. per cent and there was no albumin in the urine.

Course—On 19-5-1973 the percutaneous transfemoral (from left side) aortography was done, 20 ml. 70 per cent aqueous solution of sodium iothalamate as contrast media was injected and a block at the bifurcation of aorta was detected. Filling defect in right renal artery was also observed, collaterals were well developed (Fig. 1).

Following the aortography, the pulsations in the left lower extremity as well as in the right lower extremity became feeble, the urine output decreased, and albumin appeared in the urine. In spite of the management the patient died of renal faialure on 1-6-1973.

DISCUSSION

Abdominal aortography was introduced in 1929 by Dos Santos and his colleagues. Among the complications of aortography described, the most important is undoubtedly anuria and renal failure (Dormandy et al., 1957). At least 12 deaths from this cause are recorded in literature (Starer and Sutton, *loc. cit.*).

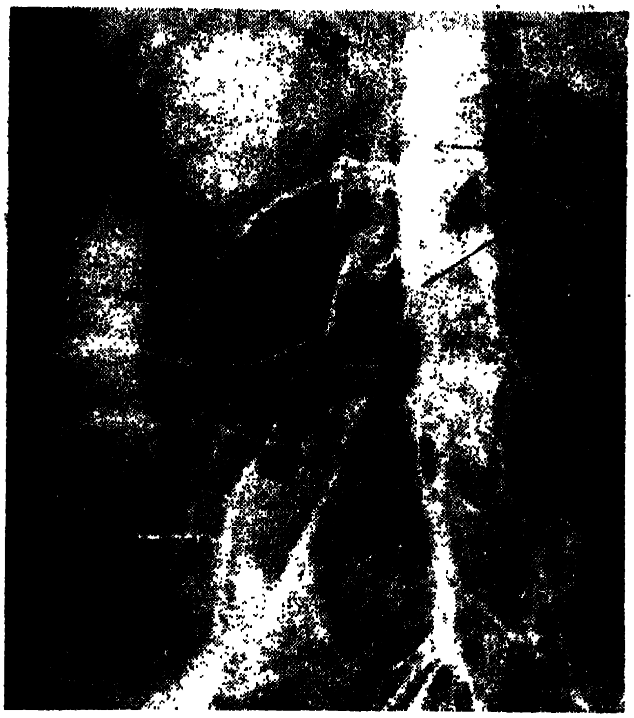

Fig. 1—Showing a Block at the Bifurcation of Aorta and Filling Defect in Right Renal Artery with Well-Developed Collaterals in Percutaneous Transfemoral Aortography

In a survey McAfee (1957) suggested that there was a greater danger of renal complications in cases of aortic thrombosis than in others. This is because with the blockage of aorta a much higher proportion of the contrast media enters the kidneys than would normally do so. Starer and Sutton (*loc. cit.*) in their larger series of cases of aortic thrombosis in which aortography was performed did not encounter any such complication. According to them there is hardly any real danger of renal damage if a dose of only 15-20 ml. of 60 per cent urografin is used. However, they have not mentioned about the blood urea in thier cases. The present case had initial blood urea 142.8 mg. per cent at the time of admission which came down to 35 mg. per cent by usual treatment and only after that the aortography was undertaken. The extra caution regarding the dose was also kept in view. In spite of that the patient manifested the clinical evidence of renal failure—oliguria, reappearance of albumin in urine and ultimately died. Though the renal pathology could not be finally evaluated by autopsy, it was quite evident clinically that the patient developed renal failure after the aortography which was otherwise fully under control.

SUMMARY AND CONCLUSION

Aortography is fairly safe but can cause renal failure in spite of reduced dose of contrast medium in cases already manifesting some evidences of renal damage like high blood urea and albumin in the urine.

A case in which fatal renal failure followed aortography in spite of reduced dosage of contrast media, is described

ACKNOWLEDGMENT

We are thankful to Dr. R. P. Chaturvedi, Principal and Controller, Jawahar Lal Nehru Medical College, Ajmer, for publication of this paper and to Dr. J. S Jhala for permitting to use hospital records.

Dianabol (Ciba) brand of methandienone tablets, conray-420 (May and Baker) brand of 70 per cent aqueous solution of sodium iothalamate as contrast media, complamina (German Remedies) brand of xantinol nicotinate were used.

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3

Treacher Collin's Syndrome

K. SRINIVASARAO*, S. SATYAMURTHI**

Treacher Collin's syndrome is a hereditary disease transmitted by a dominant gene. Treacher Collin described the essential components of this syndrome to consist of microtia, atresia of external auditory canal, malformation of middle ear bones, hypoplasia of malar and other facial bones on one side, malformation of ear, macrostomia, high palatal arch, congenital facial nerve palsy, blind fistulas deafness, atypical hair growth and antimongoloid slant. Franceschetti and Klein (1949) gave it the name of mandibulofacial dysostosis. Stovin *et al.* (1960) described 51 out of 63 cases having deformed pinna, one third of their series having defective ossicles and deafness.

There appears to be good evidence that the symptom complex is inherited as an autosomal dominant gene with marked pentrance and variable expressivity. The gene seems to have a sublethal effect for miscarriage and early postnatal death (Gorlin, 1965). But the present case is aged about 18 years and well to date. A number of families have expressed the syndrome in several generations. About 200 cases have been described to date. The present report is one such rare case report.

CASE REPORT

A female patient, aged 18 years, attended the ENT department on 2-2-1974 for her right ear deformity with intermittent slight discharge since birth, associated with defective hearing in the right ear only.

Examination—On examination, her general health was good. Local examination showed microtia of the right ear with severe degree of atresia of the external auditory meatus (Fig. 1). A probe could be passed for about 1 cm. depth only through the pinhole meatus. Below this pinhole meatus was present a rudimentary pinna, soft to touch and ugly looking and globular in appearance. Mandibulofacial dysostosis showing prominence of right malar bone and small mandible and hemiatrophy of right side of face was noted (Fig. 2).

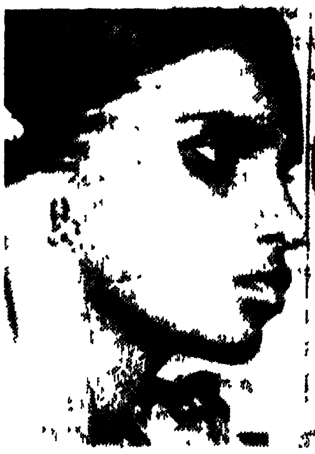

Fig. 1

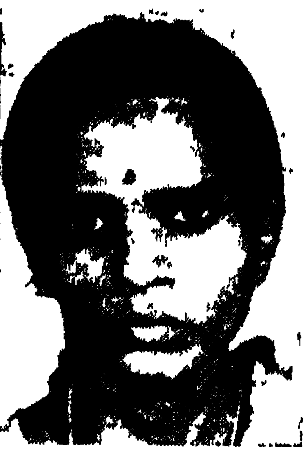

Fig. 2

Also infranuclear type of facial palsy was present on the right side since birth. The right sternomastoid muscle was prominent causing bending of the neck to the right slightly. There was no slanting of the eyes downwards nor was there any notching of the lower eyelids. No other congenital anomalies were noted. Micturition was normal. The patient was not married.

Height—148 cm., span 150 cm. Secondary sex

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characters were ill developed with small breasts and healthy external genetalia. Normal menarche started at 14th year and regular. There was no evidence of Turner's syndrome. Phenotype female, genotype female: 38 per cent positive —Barr bodies, chromosome culture 46/xx, 25 per cent positive drumsticks. She had loss of hearing and maldeveloped ear, micrognathus, hemiatrophy of right face, congenital facial nerve palsy on right side (infranuclear type), high arched palate. She was then referred to the ophthalmologist on 9-2-1974 who noted a small corneal leucoma due to old keratitis and lagophthalmos of the right eye. No active eye lesion was seen.

Family history—There was no consanguinity of the parents. There were 2 brothers and 2 sisters and she was the 4th one of the family, 2 brothers and one sister died postnatally.

Investigations—Tuning fork test—None heard in the right ear, and left ear was normal, haemogram—normal, aural discharge on culture and test for sensitivity reported sterile, blood group—'B' and urine analysis was normal. X-ray of the paranasal sinuses (P.A. view)—Right maxillary antrum was poorly visualised. Left sinuses normal. X-ray spine—C4-5 united with one spine only, and x-ray of the head and neck (lateral view)—NAD.

Surgery—On 25-2-1974, under endotracheal general anaesthesia, patient was operated upon. A vertical incision from above downwards was made into the pinhole meatus, to explore the rudimentary external auditory meatus. Skin was separated with a sharp dissector and the bony meatus of about 5 × 5 mm. was found to be present. Cartilaginous meatus was absent. Operating microscope was focussed now towards the annulus tympaniens. The tympanic membrane appeared to be very small, opaque, and the mallear attachments could not be discerned. The skin of the floor was found to be eczematous in the meatus probably due to ill advised scratching by the patient. Tympanotomy was thought unnecessary at this stage as the patient was having normal hearing in the opposite ear. The wound was closed with suitable sutures and dressed. The auricular remnant was then excised by an eliptical incision at its base and the wound was closed with suitable sutures. Post-operative recovery was normal. The need for fitting an artificial auricle was considered and the patient was advised to come after some time for the same. The excised tissue was sent for histopathology and the report was—complete absence of cartilage but only fibrous tissue present.

COMMENTS

The facial appearance of this case is quite characteristic of Treacher Collin's syndrome. The downward sloping palpebral fissures, sunken cheek bones and deformed pinna, receeding chin and large fish like mouth present a clinical picture that once seen is unforgettable.

Skull—The calvarium is normal but x-ray studies revealed that the supra-orbital ridges are poorly developed. The body of the malar bones may be totally absent but more often undeveloped. The mastoids and maxillary antra are not pneumatised and frequently sclerotic. The paranasal sinuses are small or absent.

Ear—The pinna is often deformed, crumpled forward or misplaced. Stovin *et al.* (*loc. cit.*) described in their survey that 51 out of 63 cases had deformed pinna and ⅓rd had defects of ossicles accompanied by deafness. X-ray studies showed sclerosis of the middle and inner ear with poor dilineation of their structure. The auditory ossicles and vestibular apparatus were observed to be absent. Surgical exploration revealed absence of inner ear ossicles and oval window, complete absence of middle ear and epitympanic space, extra ear tags, serosanguineous discharge from non-canalised external ear was noted in presence of congenital facial paralysis. Gross tympanomastoid abnormalities are to be found (Mishra and Shukla, 1974). Because of the poor development of the maxilla and the frequency of high arch or cleft palate, dental malocclusions are frequent and the teeth may be arranged jig jag, widely separated or displaced.

Gorlin (*loc. cit.*) described this as autosomal dominant but in the present case, since none of the parents of the propositus showed the character, it might be due to mutation. Such mutational changes in Treacher Collin's syndrome were not described in the literature so far available and hence being reported.

SUMMARY

A rare case of autosomal dominant Treacher Collin's syndrome is presented here. In the present case the character is due to autosomal mutation.

Mandibulofacial dysostosis is prominently noted and the review of the literature studied.

The Indian literature on this syndrome is rare.

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JOURNAL OF THE
INDIAN MEDICAL ASSOCIATION

CALCUTTA, JANUARY 1, 1975

Multiple Sclerosis

Multiple sclerosis is the most common demyelinating disorder. It is a disorder of unknown aetiology, characterised pathologically by widespread patches of demyelination followed by gliosis in the nervous system. The first pathological account of the disease was given by Cruveilhier in 1835 and Carswell in 1838. There are a number of well recognised syndromes, but border line cases may be difficult to categorise clinically and pathologically. It is a chronic and irregularly progressive disorder. often characterised early by acute remittent phases of neurologic dysfunction.

The fluctuations in the incidence of multiple sclerosis in different parts of the world continue to attract attention. Many workers[1-3] have drawn attention to the prevalence of the disease in cold and temperate climate. But prevalence of this disease in India is not insignificant[4, 5]. This has been our experience also. The disease affects males and females about equally. In two-thirds of all cases it begins between 20 and 40 years of age, rather more often in the third than in the fourth decade.

Genetic studies have not elucidated the cause of multiple sclerosis. Instances of multiple sclerosis occurring in families have been shown by some workers. Pratt *et al.*[6] found an incidence of 6.5 per cent with a family history of the disease. This is much lower than that found in cases of diseases in the aetiology of which heridity is the principal factor. The possible effect of genetic factor in multiple sclerosis has also been studied[7].

A large variety of events immediately precede the onset of the illness and have often been regarded as a precipitating factor though their mode of operation is unknown. They include influenza and infection of the upper respiratory tract, the specific fevers, superficial sepsis, surgical operations, extraction of teeth and pregnancy. About 10 per cent of the cases give the history of non-specific type of infection preceding the onset of the disease[8].

While the better control of bacterial infections has resulted in a decline of certain postinfective disorders, such as, acute rheumatism and nephritis, there appears to have been no corresponding drop in frequency of new cases of multiple sclerosis[9].

Trauma requires special consideration as important issues, both scientific and legal, may arise from it. History of trauma preceding the onset of symptoms by less than 3 months was obtained in 14.4 per cent[10] of cases, but in only 5.2 per cent of controls. Trauma may thus precipitate the disease. We cannot say whether it initiates it, in the sense that apart from trauma the disease would never have occurred. The conclusion reached by the associate of research in nervous and mental diseases in 1922 was as follows : "In a small percentage of cases of multiple sclerosis it appears to be excited by trauma. but trauma cannot itself cause it, but may apparently awaken a disease process potentially existent"[8].

Many workers have stated that pregnancy aggravates the disease, but this is open to question. The disease and pregnancy occur in the same age group. The potential harmful effect of puerperium on multiple sclerosis patient, should lead to fresh thinking on measures[11] that should be taken to lessen the risk of fatigue. Pregnancy is generally considered non-deleterious to the course of multiple sclerosis in any patient who has not had an attack in two years.

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The acute lesions of multiple sclerosis consist of circumscribed areas in which the myelin sheath have undergone destruction while the axis cylinder shows irregular swelling. Infiltration by microglial phagocytes and mononuclear cells are seen around vessels, as well as scattered in the lesion itself. As the lesion becomes chronic, there is proliferation of glial cells giving rise to 'sclerotic plaques'. The axons in these areas may be preserved or destroyed. The lesions are well scattered in the white matter of the brain, spinal cord and in the optic nerves. The natural history of the disease produces a very varied clinical picture. In the early stages it is often that of a single focal lesion. As time goes on, the culminating effects of earlier lesions constitute a persistent background of incapacity upon which fresh disabilities due to new lesions are superimposed. The initial clinical feature develops fairly suddenly and disappears after a few days or weeks.

The weakness usually begins in the lower limbs but upper extremities may also be involved. The weakness may be minimal, or there may be total paralysis. Spontaneous jerks of the legs, while at rest, are common in the early stages. Usually, pyramidal signs such as spasticity with increased deep reflexes and extensor plantar response with depression or absence of the abdominal reflexes are met with. Occasionally, in multiple sclerosis the abdominal reflexes are absent with flexor plantar responses, in association with exaggeration of deep reflexes. This finding, if confirmed, is significant in a young person. Motor weakness is the most common mode of presentation[12, 13]. When both the lower limbs are involved, urinary complaints such as urgency or frequency may be present.

Visual complaints include blurring of vision with a central scotoma and diminished visual acuity or diplopia with paresis of the extraocular muscles and nystagmus. There may be pain on movement of the eyeballs. A mild papillitis with peripapillary oedema may occur. It is due to a lesion close to the nerve head. Pain or headache is usually prominent, and the depression of central vision is severe, contrasting with the normal vision observed in early papilloedema due to increased intracranial pressure. The vision usually recovers in two to three weeks, though partial scotoma may persist, and pallor of the temporal half of the disc may subsequently appear.

Paraesthesia may involve one or all the extremities. Usually, there is impairment of vibration and position sense in the lower extremities, whereas cutaneous sensation is relatively spared. Mental changes, such as euphoria, may occur in some cases. Cerebellar lesions cause nystagmus, intention tremor, ataxia and dysarthria. Multiple sclerosis affecting the brain stem may give rise to varied symptomatology. If the disease begins acutely in the frontal lobes, psychic disturbances may lead to considerable diagnostic difficulties.

The abnormal findings in multiple sclerosis are usually confined to the cerebrospinal fluid. This is present in at least half of the cases. In the acute disease, there may be mild lymphocytosis. The protein is usually normal or only slightly elevated. The gammaglobulin content in the cerebrospinal fluid is elevated[14] and correspondingly, there is often an abnormal colloidal gold curve (first or second zone) accompanied by a negative serological test for syphilis.

The electro-encephalogram may be mildly abnormal, revealing either focal or generalised abnormalities, but it is in no way diagnostic.

Work is now progressing on the auto-antibody studies in multiple sclerosis and only the future may show what light it may throw on the diagnosis of this disease.

There is no specific treatment. The general management requires tact and judgement. The beneficial effect of ACTH or of corticosteroids during an acute exacerbation is now well known. This may be given for three to four weeks. There is no indication for a long term maintenance therapy with ACTH or corticosteroids, and the risk outweigh any possible benefit. Immunosuppressive agents have been used with little success. Symptomatic treatment may be given as necessary. During a relapse, the patient should be confined to bed but prolonged immobilisation must be avoided. A well planned physiotherapy and occupational therapy are of great value.

P. K. SEN

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CURRENT MEDICAL LITERATURE

Oestriol Assays on Single Specimens of Urine in Pregnancy

CAHILL, S. C., MAGNER, J. W., and RITCHIE, E. H. (*J. Irish Med. Ass.*, **67**: 314, 1974) from the Department of Pathology, Bon Socours Hospital and Erinville Hospital, Cork, write:

The measurement of oestrogen in a 24-hour collection of urine is a well-established test of foetoplacental function. However, use of the test is limited in two ways. Firstly, 24 hours are required to collect the urine and so the result cannot be obtained quickly. Secondly, if the patient is an out-patient there may be uncertainty whether the 24-hour collection is complete. If a single specimen of urine could be used in place of the 24-hour collection both these limitations would be avoided.

Sixty-seven patients with suspected placental insufficiency were studied. Oestriol and creatinine were measured in 112 mid-morning single specimens of urine and in 112 concurrent 24-hour collections of urine.

The E/C ratio (mg. oestriol per g. creatinine) of the single specimens was compared with the mg. oestriol in the concurrent 24-hour collection of urine.

In 109 tests (97.3 per cent) the E/C ratio in the single specimen of urine was less than 10 above the mg. oestriol in the concurrent 24-hour collection and in 95 tests (84.9 per cent) the E/C ratio in the single specimen was less than 5 above the mg. oestriol in the concurrent 24-hour collection.

Measurement of the E/C ratio in mid-morning single specimens of urine gives a reliable estimate of the oestrogen excreted in a concurrent 24-hour collection of urine. This test should be considered when an estimate of foetoplacental function is needed quickly, and is likely to be of particular value in the screening of ante-natal out-patients.

Copper Metabolism and Wilson's Disease

GOLDSTEIN, N. P. and OWEN, C. A. (*Proc. Mayo. Clin.*, **49**: 363, 1974) from the Department of Neurology and Medical Sciences Biochemistry, write:

The diagnosis of Wilson's disease (WD) in the typical patient, especially with Kayser-Fleischer rings, now is straightforward, and the treatment with D-penicillamine and a low-copper diet is reasonably effective. But questions remain to be answered. The newborn infant exhibits some of the characteristics of WD—increased concentration of copper in the liver and low level of ceruloplasmin in the plasma. Both of these convert to normal within a few months. Is WD the result of a failure of this conversion?

Although the serum ceruloplasmin concentration usually is seriously depressed in WD, does the lack of this copper-enzyme lead to development of the disease? The only known function of ceruloplasmin is to mobilise iron from storage organs. But anaemia, although often present in mild form, is far from the main problem in WD. Are there other functions of ceruloplasmin more directly related to WD? Or is the hypoceruloplasminaemia merely a manifestation of some more fundamental problem? It has been suggested that the tissues of patients with WD have an usual avidity for copper, which could account for the progressive accumulation of this metal in the liver, kidney, brain, and cornea. Yet, severe copper intoxication can be induced in experimental animals and results in selective copper-loading in the kidney, liver, and brain—all without decreasing the concentration of ceruloplasmin in the plasma and without the manifestations of WD.

Leucocyte Function in Protein Deficiency States

WELFSDERE, J. and NELAN, R. (*S. Afr. Med. J.*, **48**: 528, 1974) from the Department of Paediatrics and Child Health, Godfrey Huggins School of Medicine, University of Rhodesia, Salisbury, Rhodesia, state:

Seventy-five patients, comprising 3 groups of 25 normal infants (group I), 25 infants suffering from protein energy malnutrition (PEM—kwashiorkor) (group II) and 25 infants with PEM plus infection (group III) were examined, with particular reference to their total leucocyte count and the response of their white cells to incubation with nitroblue tetrazelium (NBT), with and without latex particle stimulation. No difference in leucocyte counts could be demonstrated between the groups; however, both groups of malnourished patients (groups II and III) had elevated NBT levels, although no difference could be detected between those malnourished infants with and without clinical or laboratory evidence of infection, or both. The data indicate that although primarily protein-deficient malnourished patients have a quantitative deficiency in leucocyte response, qualitative leucocyte function may be normal.

Hodgkin's Disease

EWING, D. P., ROZENBERG, M. C., FREEDMAN, A., GRACE, C. S. and LAM-PE-TANG, P.R.L.C. (*Med. J. Aust.*, **2**: 128, 1974) from Institute of Radiotherapy, Prince of Wales Hospital, Sydney, write:

The management of 122 patients with Hodgkin's disease seen at the Prince of Wales Haemio-Lymphatic Clinic between 1968 and 1972 is described. All underwent the investigations now recognised as necessary to establish the stage of the disease, and 38 underwent staging laparotomy. Sixty-eight patients were treated initially with radiation therapy and a relation between the early stages and longer survival was apparent. Thirty-seven patients started quadruple therapy with a significant improvement in 26. The advantages of a multi-disciplinary approach to the treatment of Hodgkin's disease are emphasised.

Digitalis Toxicity

MILLER, S. and FORKER, A. D. (*J. Kansas Med. Soc.*, **75**: 263, 1974) from the Department of Internal Medicine, Wesley Medical Centre, Wichita, Kansas and from the Department of Medicine, KIMCWSU Branch, 2221 N. Hillside, Wichita, Kansas, comment:

Differential diagnosis of an acute brain syndrome or delirium should always include drugs, even cardiac drugs such as digitalis.

The non-cardiac symptoms of digitalis intoxication have been recognised since the initial report of Withering. Most physicians recognise that anorexia, nausea, vomiting, and visual complaints—especially abnormalities in colour vision, are associated with digitalis intoxication. However, other CNS toxic effects of digitalis are less well known. Neurological symptoms may be the earliest, the most severe, and sole manifestation of digitalis toxicity.

In addition to visual symptoms, Batterman and Gutner described the following neurologic manifestations of digitalis toxicity; vertigo, headache, drowsiness, restlessness, irritability, delusions, disorientation, delirium, depression, temporary amnesia, peripheral neuralgia, aphasia, stupor, coma, and convulsions. These symptoms usually were present in older adults.

In summary, the patient presented in a confused, delirious state associated with a diffusely abnormal electro-encephalogram; he had a very high serum digitoxin level (85 ng./ml.), and his symptoms were totally reversible following withdrawal of digitoxin. No underlying cardiac disease was present. The common digitalis toxic symptoms of nausea, vomiting, and visual difficulties were absent. The clinical clue to the presence of digitalis intoxication was the electrocardiographic finding of A-V dissociation, and later second-degree A-V block.

Electro-encephalogram in Minimal Cerebral Dysfunction

MURDOCH, B. D. (*S. Afr. Med. J.*, **48**: 606, 1974) from Neuropsychology Division, National Institute for Personnel Research, CSIR, Johannesburg, observes:

Electro-encephalograms (EEGs) of 35 children at a centre for remedial education and 35 age- and sex-matched normal controls at a private school were recorded on two occasions, with an 8-month interval, during which the minimal cerebral dysfunction (MCD) group received specialised remedial instruction, and the control group normal class-room schooling. The EEGs of each group were compared both before and after the 8-month period. The results of previous investigations showing that children with MCD have a significantly higher incidence of EEG abnormalities of a slow wave type, were confirmed. Further, the MCD group differed from the control group on a number of measures related to alpha activity, and showed a significantly greater subcortical excitability. Right posterior EEG dysfunctions were implicated in a significantly higher proportion of the MCD group and appeared to be related specifically to reading disability. Difference between control and experimental groups were reduced after the 8-month period between EEGs, suggesting that a process of normalisation was operative in the MCD children.

Carcinoembryonic Antigen in Rheumatoid Arthritis

UNGER, A., PANAYI, G. S. and LESSOF, M. H. (*Lancet*, **1**: 781, 1974) from the Department of Medicine and Guy's Arthritis Research Unit, Guy's Hospital Medical School, London, state:

Carcinoembryonic antigen (CEA) levels measured by radioimmunoassay were significantly higher in adults with seropositive rheumatoid arthritis (18 cases) than in those without inflammatory disease (17 subjects). 10 patients with seronegative rheumatoid arthritis and 16 with ankylosing spondylitis had levels of plasma CEA which did not differ significantly from the control group. Synovial fluid from 8 RA patients was assayed. In 4 cases the level of CEA in the synovial fluid was more than three times higher than in the plasma. In the remaining 4 cases there were less striking differences. Further studies may help to assess whether inflammatory change in the synovium leads to reactivation and expression of a foetal antigen and whether the CEA level in rheumatoid arthritis changes with treatment or with the activity of the disease.

Phagocytes and Hyperalimentation

CRADDOCK, P. R., YAWATA, Y., VANSANTEN, L., GILBERSTADT, S., SILVIS, S. and JACOB, H. S. (*New Eng. J. Med.*, **290**: 1403, 1974) from the Department of Medicine, University of Minnesota Medical School, The University of Minnesota Hospitals, and the Minneapolis Veterans Administration Hospital, write:

Cachectic patients infused with hypertonic amino acids and dextrose (parenteral hyperalimentation) are subject to severe hypophosphataemia and recurrent fungal and bacterial septicaemia. We observed a relation between the two. Severe hypophosphataemia, induced in a total of 18 mongrel dogs, resulted in a 50 per cent depression of chemotactic, phagocytic and bactericidal activity of their granulocytes. There was a concomitant reduction in leucocyte ATP content. The motility defect was corrected if cellular ATP was repleted by phosphate supplementation of animals *in vivo* or by incubation of leucocytes with adenosine and phosphate *in vitro*. Analogously, severe hypophosphataemia in a hyperalimented patient was associated with a 45 per cent impairment of chemotactic responsiveness and was reversed by similar *in vivo* and *in vitro* manipulations. The studies provide an additional explanation for the high rate of sepsis in patients undergoing hyperalimentation therapy, secondary to an acquired granulocyte dysfunction induced by hypophosphataemia.

CURRENT TOPIC

Nobel Prize Winners in Medicine (1974)

RANAJIT KUMAR DATTA*
BHAKTI DATTA**

In recognition of their innovations that largely laid the foundation of the modern science of cell biology nearly 30 years ago and for their major contributions since to the knowledge of the inner working of living cells two naturalised US scientists and one Belgian scientist have been awarded the 1974 Nobel Prize for Medicine/Physiology. The awardees who will share equally the $124,000 cash prize are Dr. Albert Claude, 75 years, Director of Jules Bordet Institute in Brussels, Dr. George Emil Palade, 61, Professor of Cell Biology of Yale University School of Medicine in New Haven and Dr. Christian Rene de Duve, 57, Professor of Cell Biology at Rockefeller University in New York and at the University of Louvain in Belgium. The prize winning works of all the three scientists were started and carried out largely at Rockefeller University.

The Royal Caroline Institute in Stockholm which had chosen the awardees cited them as pioneers in the understanding of the subcellular physiology of living cells and in providing many other researchers with ideas to work on more selective ways to treat diseases that may arise from problems in subcellular components (organelles) such as mitochondria, microsomes, ribosomes, endoplasmic reticulum, lysosomes and peroxisomes which these awardees identified, isolated and characterised. A new branch of subcellular pathology emerged from these awardees' works in subcellular physiology. Idea is now growing that the pathology of a tissue or its cells is the pathology of its subcellular components. Because most medical treatments for disease aim at gross abnormalities seen in whole tissue rather than at detailed subcellular abnormalities in some diseases, at least, the therapy is far from being adequate and specific. The growing knowledge of subcellular pathology appears to hold promise for adequate and localised therapy at the subcellular level. Time is coming for the application of cell biology to everyday medicine for practical benefit for patients, Dr. de Duve believes. Electron microscopic examination of tissues, particularly renal and liver biopsies, is made routinely in large hospitals in the USA. Thirty years ago such approach to medicine would have been nearly impossible; ordinary light microscopy simply fails to reveal the complexity of a cell with its tiny organelles. This year's award of Nobel Prize to Drs. Claude, Palade and de Duve marked recognition of cell biology as an important discipline of bio-medical science. In recent years, the Nobel Prizes were awarded to a number of molecular biologists whose works largely utilised methods which this year's awardees developed in isolating organelles with which the molecular biologists worked. In 1970, the Columbia University's prestigious $25,000 Louisa Gross Horwitz Prize was awarded to Drs. Palade, Claude and Keith R. Porter for their contributions to the knowledge of the function and fine structure of cellular materials.

Of the three awardees, the recognised senior scientist is Dr. Claude, who was the first to apply the electron microscope to the study of cells and to use a centrifuge to separate out various organelles of cells for study of their morphology and functions. In fact, Dr. Claude identified mitochondria and endoplasmic reticulum electron microscopically in early forties. Other two recipients capitalised upon Dr. Claude's methods and devices and refined them for more reliable and accurate biochemical analyses of the organelles. They discovered and studied the functions and morphology of other cell organelles such as microsomes, ribosomes, lysosomes and peroxisomes. As a result of their studies, cells are known to have a variety of specialised internal organelles which are able to digest nutrients from outside, repair their internal damage, synthesise small and high molecular weight substances, regulate metabolism, both anabolic and catabolic, destroy germs invading germs in highly specialised ways. These organelles are capable of doing most of these functions in *in vitro* cell-free systems.

Dr. Claude, in early forties, at Rockefeller University (then known as Rockefeller Institute for Medical Research), while attempting to learn what cancer viruses did when they invaded normal cells, seized upon the electron microscope, which was then invented a few years earlier, believing that its ability to see much smaller objects might help. Only physicists and metallurgists used the electron microscope then. In 1945, he succeeded and published the first detailed morphology of a cell, revealing a number of subcellular structures such as mitochondrion, which is cell's energy factory, and endoplasmic reticulum, a network of fibres that structurally supports other organelles. Further, Dr. Claude and his colleague Dr. Keith R. Porter (now Chairman of the Department of Molecular, Cellular and Developmental Biology at the University of Colorado at Boulder) were the first to view, by the electron microscope, the presence of cancer virus particles in tumour cells. While continuing his work with electron microscope, Dr. Claude developed centrifugal fractionation of

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**M.B.B.S., D.G.O., Dip. Pathol. (U.S.A.), Associate Pathologist, St. Barnabas Hospital for Chronic Diseases, Bronx, New York cell's components with the objective of separating and studying biochemically what he observed electron microscopically. By grinding and preparing a homogenate of whole cells and then spinning it down in a centrifuge Dr. Claude obtained many layers of differing particles, which upon further spinning gave pure organelles—ready to study, in cell-free systems, of their morphology, biochemical functions and physical properties.

After the World War II Dr. Palade joined Dr. Claude at Rockefeller University. Working with the electron microscope he developed new techniques for preparation of specimens that are now in use in electron microscopy. Dr. Palade also developed high-speed centrifugation and obtained relatively purer organelles free from contamination. The biochemical analysis and the electron microscopic morphology provided a relatively complete description of many of the organelles. One of his more significant discoveries was the ribosome, the tiny organelle supported by the endoplasmic reticulum Dr. Claude found. The ribosome is also called Palade granule. Ribosome is cell's protein-synthesising factory.

Dr. de Duve fractionated cell components in centrifuge and assayed their biochemical properties and enzymic profiles. Therefrom he concluded that each organelle was characterised by its biochemical constituents and enzymic profiles, and that organelles could be distinguished by such assays. The electron microscopic studies confirmed the organelles predicted by biochemical and enzymatic characterisation. One of his more significant discoveries was the lysosome —the tiny particle filled with several hydrolytic enzymes. The lysosomes take in and break down foreign materials such as bacteria invading the cell. In 1955, Dr. de Duve and his associates reported that a group of hydrolytic enzymes active in acidic pH was concentrated in the light mitochondrial fraction isolated from liver homogenates of rat by differential centrifugation. The enzymes were thought to be belonging to a special type of cytoplasmic granule, 0 2 to 0.4 micron in diameter, and to function in the lysis (degradation) of various biological substrates. Dr. de Duve called them lysosomes. He and his associates also observed that the hydrolytic enzymes of the isolated lysosomes were active only if these granules were damaged by osmotic shock, freezing and thawing or by detergents and that lysosomes were surrounded by a membrane of lipoprotein nature restricting the accessibility of external substrates to the internal enzymes. The discovery of lysosomes soon gave rise to new ideas of linking lysosomes and phagosomes to ingestion process, phagocytosis, autolysis, autophagy, immune process, inflammation, necrosis, shock and virus infection.

In 1964, Dr. de Duve and his associates succeeded in separating a rat liver mitochondrial fraction, by density gradient centrifugation, into three distinct groups of organelles: mitochondria, lysosomes and a new type of particles containing urate oxidase, catalase and D-amino acid oxidase. The subcellular distribution of these three enzymes was difficult to elucidate; they were neither mitochondrial nor lysosomal. Dr. de Duve's use of injections of a neutral detergent Triton WR 1339 produced massive swelling of the lysosomes, but was without effect on the urate oxidase-catalase-D-amino acid oxidase-containing particles. By this means, Dr. de Duve and his associates obtained a reasonably pure fraction of these particles. The electron microscopy revealed that these liver particles had the characteristic morphology of the so-called microbodies previously described by others in 1956. These particles were slightly smaller than mitochondria, had a single bounding membrane and contained a characteristic central core. In 1966, Dr. de Duve proposed the term peroxisomes for the microbodies and suggested that peroxisomes had an important role in extra-mitochondrial oxidation for removal of reduced nicotinamide adenine dinucleotide (DPNH) produced in the cell sap.

Born in August, 1899 in Luxembourg, young Claude grew up and attended schools in Belgium. In 1929 when he just completed his medcal education in the University of Liege he received a Government scholarship for overseas study at New York's Rockefeller Institute for Medical Research. He was associated for 20 years with Rockefeller Institute where he, using the first electron microscope available for bio-medical studies, in New York City, made the first successful application of that instrument to the study of cells and then developed centrifugation method to separate cell components. In 1950, Dr. Claude returned to Belgium and for the next 20 years built a cancer research centre at the University of Belgium. He retired from there several years ago and now heads the Jules Bordet Institute in Brussels.

Born on November 19, 1912, at Jassi in Rumania, young Palade had his medical degree from the Bucharest Medical School (1940) and taught anatomy there. In 1946, he came to the Rockefeller Institute as a visiting investigator to work with Dr. Claude. There he became Assistant (1948-51), Associate (1951-53), Associate Member (1953-58), Member and Professor of cytology (1958-64), and Professor of cell biology (1964-72). In 1972, he left Rockefeller University to take over the Cell Biology Department of Yale University School of Medicine. Recipient of the Lasker Award for Basic Medical Research (1966) and the Louisa Gross Horwitz Prize (1970) Dr. Palade is a member of the US National Academy of Sciences.

Born on October 2, 1917, in England, young de Duve received his medical degree from the University of Louvain in 1941. While continuing his graduate work there he earned a master degree in chemistry in

1946. He left Belgium and worked in the Nobel Institute and the Carl Cori Institute of St. Louis' Washington University before returning to the University of Louvain. In 1962, Dr. de Duve accepted an appointment to work part-time at Rockefeller Institute. Honoured by several universities in Europe and the USA Dr. de Duve authored a book entitled "Glucose and Insulin in Diabetes" (1945). He is also renowned for his research on carbohydrate metabolism, particularly the action of insulin and glucagon in diabetes.

NOTES AND NEWS

Centre's Warning against Dengue

Government of India has sent special instructions to State Governments on measures they should take to prevent the spread of dengue haemorrhagic fever, the Lok Sabha was recently told There were 3,011 cases of dengue during the year 1974. In Rajasthan alone, 2,138 cases were reported between January and July. Giving this information in the Lok Sabha, Dr. Karan Singh, Union Health Minister, said it was for the State Governments to remain active, and the Centre had no proposal to give any special grants to them to control the fever.

Bombay Doctors Alarmed at Spurt in Spurious Drugs Supply

Alarmed over the serious situation created by the acute shortage of genuine drugs and flooding of market with spurious and substandard stuff hundreds of doctors of Bombay recently met and passed a resolution urging the Prime Minister to take immediate steps to see that sufficient quantities of reasonably-priced quality drugs were manufactured and made available all over the country.

The resolution suggested that all competent drug manufacturers should be encouraged to maximise their production and manufacturers and distributors of spurious and substandard drugs should be punished.

Role of Radiation Sterilisation

Radiation sterilisation has an important role to play in upgrading medical products made locally to help in improving health care and in fostering indigenous industry.

This consensus was arrived at the concluding session of the international symposium on Ionising Radiation for Sterilisation of Medical Products and Biological Tissues at the Bhabha Atomic Research Centre in Bombay.

The participants said that radiation sterilisation was superior to other methods of sterilisation such as ethylene oxide sterilisation, which had several drawbacks.

Vitamin C Helps to Keep Arteries Clean

Hardening of the arteries (atherosclerosis) which leads to heart attacks is a disease caused by vitamin C deficiency, according to work done at the Pinderfields General Hospital in England.

Dr. Constance Spittle of the hospital has found that vitamin C keeps the arteries clean by preventing deposition of the fatty cholesterol. It also helps in transporting cholesterol from arteries to the liver, for conversion into bile acids.

The conclusion is based on a trial carried out on 25 atherosclerotic patients. The trial showed that when vitamin C is low, cholesterol in the blood moves to the heart, where it gets deposited in the arteries.

"By keeping the cholesterol moving in the right direction, by enhancing the metabolism of cholesterol once it is in the liver, and by maintaining the arterial walls in good repair, vitamin C can keep arteries clean," it is claimed.

For people with confirmed or suspected atherosclerosis, Dr. Spittle has recommended one gram of vitamin C per day. For others half a gram a day is enough to keep their arteries clean—*BIS*.

Immunotherapy Proves Promising in Breast Cancer Treatment

Immunotherapy has shown promise for an effective treatment of breast cancer, according to a team of medical scientists in New York. In a report on the proceedings of the National Academy of Sciences Dr. H. Sherwood Lawrence and colleagues state that they took a certain chemical from the lymphocytes of women aged between 40 and 65 years, and with no history of cancer, and injected it into five women with advanced breast cancer. The treatment, they note, "boosted the cellular immunity in all the patients and triggered cancer regression for six months in one patient." None of the subjects reported any side effects.

Skin Institute, New Delhi, Invites Entries for Its Annual Prizes

The Skin Institute of New Delhi has announced the following prizes:

i) Annual prize of Rs. 1,000/- to a worker preferably below the age of 50 years for original work done on 'Dermatological therapy'. The article should not exceed 15 typed pages (approximately 3000 words) in double space on foolscap paper excluding charts and diagrams. An article or a paper already published will not be considered.

ii) Annual prize of Rs. 500/- for publication of best thesis by postgraduate students in Dermatology. The work should be forwarded through the Professor of Dermatology to the Director, Skin Institute.

The last date for submitting entries for the prizes is *31st March, 1975*. The entries should be sent to Director, Skin Institute, 5A Mathura Road, Jangpura, New Delhi 14.

CORRESPONDENCE

The Editor is not responsible for the views expressed by correspondents

Counter-Irritation—Chinese Style

SIR,—I went through the interesting article on "Counter-Irritation—Chinese Style" (*J. Indian M.A.*, **62**: 389, 1974). It is a new type of case in country like India. The presence of congestion of all organs in abdomen, with bronchopneumonic consolidation and the evidence of meningitis with seropurulent exudate on surface and base of brain, naturally leads to the diagnosis as suggested in the article.

Looking to the other side of the coin one notes the presence of all the superficial injuries on ventral and lateral aspects of the body of a girl of rapeable age. One may presume that her father who might be practising some system of medicine, having probably been disgusted with the past history, took a decision (when the child was sick) to finish her off. (1) During the struggle, she must have had mild concussion (over a pathological intracranial structures), even a slight injury to brain (vital organ) could kill her. (2) An intravenous narcotic (no mention is made in the article for its special search) could kill her. (3) Over a mild concussion a good dunlopillo-like soft pressure over nose and mouth (without injuries) could kill her. However, it being a peculiar case, out of interest at least the viscera should have been preserved to rule out the probable poisoning. All those signs mentioned in the article could be present in asphyxia or poisoning.

I have another interesting difficulty in another type of medicolegal case.

A sharp pointed ice-cone mounted over a pistol or a gun is aimed and shot at heart within firing range. The ice produces a sharp cutting injury and melts. The missile (bullet) falls out before touching skin without producing burnt and charred injury. The medico, who conducts post-mortem examination, opines "injury is due to sharp cutting pointed instrument". How should a medicolegal expert help prosecution to arrive at a leading clue ?

I am, etc.,

Civil Hospital, K. G. KULKARANI, M.B.B.S.
Dharwar. Resident Medical Officer

* * * *

SIR,—Dr. K. G. Kulkarni being not fully convinced about the diagnosis on autopsy examination has presumed some other possibilities likely to have caused the girls' death.

The police investigation and personal interrogation of the relatives of the deceased revealed that the girl was running high temperature, etc., for the last three days prior to her death. The history and course of the disease conformed to the diagnosis of meningitis associated with bronchopneumonia as was noticed on autopsy examination. There were no such signs on autopsy examination either to substantiate or even to suggest the contention of causing concussion by head injury or producing asphyxiation by smothering,—not to speak of rape or any attempt at doing so. Chemical examination of the viscera (which was done but whose report was received later) did not reveal any evidence of poisoning.

It is the common observation in medicolegal parlance that the murderer always applies more force than is required to kill his victim and usually some evidence is left to help to connect the crime with the criminal. I had no occasion to discount this observation during my 20 years of work in this field of medical discipline.

The problem as propounded in the later part of the letter lacks in specific details. An automatic pistol or a service revolver, not to speak of a rifle, when fired from a close range on an unclothed body on bare skin over the precordium, will produce typical gunshot wound of entrance with all its plausible features even when the cone of ice remains mounted on the muzzle end of the weapon at the time of firing.

An experienced medicolegal expert should really have no problem with such a type of medicolegal case.

I am, etc.,

J. B. MUKHERJEE, M.B.B.S.
Upgraded Department of Ph.D.(Lond.), M R C. Path.(Lond.),
Forensic and State Medicine D.M.J.(Lond.), F.A.F.Sc.
Medical College, Calcutta. Professor and Head

REVIEW

Assessment of the Carcinogenicity and Mutagenicity of Chemicals—Report of a WHO Scientific Group, (WHO Techn. Rep. Ser. No. 546), World Health Organisation, Geneva, 1974, 20.3 cm. × 14 cm., pp. 19, Sw. Fr. 4.

From various laboratory investigations it has been revealed that a number of environmental chemicals and food additives are carcinogenic or mutagenic, even at low concentrations. Initially, the WHO Scientific Group convened meetings from time to time to discuss the various aspects of these carcinogens and mutagens, specially as health hazards and observed that there are considerable difficulties in determining the risks to man. During last two years a number of new testing procedures have been developed and more useful data have been obtained. On the basis of these information, the WHO Scientific Group convened a meeting in 1973 to discuss the assessment of carcinogenicity and mutagenicity of chemicals likely to be present in the environment, the proceedings of which has been very well represented in this report.

The present knowledge of machanisms of mutagenesis and carcinogenesis and their interrelationship have been very clearly discussed. It is essential for many compounds to be activated either by tissue enzymes or by enzymes of the intestinal flora before they exert a carcinogenic or mutagenic action. Bearing this in mind new techniques have been evolved by introducing *in vitro* system of bio-assay incorporating metabolic activators which can be considered a significant advancement in the test system. It has been observed that although some potent mutagens have not been demonstrated as carcinogenic in any of the test systems used and not all carcinogens as mutagenic, there are evidences that in their carcinogenically reactive form many carcinogens can induce mutations. Point mutations have mostly been reported from studies in microbial system whereas chromosomal abnormalities have been observed in tissue culture and more recently *in vivo*. Carcinogenicity, on the other hand, is reported largely from *in vivo* studies in rodents. However, WHO Scientific Group agreed that no single test system can detect and characterise all mutagenic agents and therefore the use of several tests is desirable.

In dealing with the determination of threshold for carcinogenic hazards the report discussed a number of arguments against the existence of such a threshold including the summation effect described by Druckrey. However, the report emphasised that the existence of a threshold may be envisaged, and proposed a procedure for assessing the health hazard of carcinogens at a very low level of exposure, the details of which has been given in an annex.

The recommendations of the Scientific Group in regard to various approaches and procedures for assessing the risk of low-level carcinogen exposures are undoubtably valuable.

SANTOSH MITRA

OBITUARIES

Dr. R. N. Thukral

Dr. R. N. Thukral, a member of the Delhi Medical Association, passed away on 20-2-1974 following a heart attack.

Born on 2-1-1902 at Saruki in the Gujral district (now in Pakistan), Dr. Thukral qualified for the profession from the Agra Medical School in 1922. He joined the then army medical service and served at different fronts during the Second World War.

In free India he participated in Hyderabad operations of the Indian army. He retired from military service in 1952 and started practice at Karol Bagh, New Delhi. Besides earning popularity as a physician, he also served as medical officer to a number of schools in Delhi and endeared himself to the children in a big way.

He leaves behind his wife, three sons and three daughters.

DR. R. N. THUKRAL

DR. M. N. DUTTA

Dr. M. N. Dutta

Dr. Monmotho Nath Dutta of Kulti passed away on 3-11-1974. He was 76.

Born in a poor agriculturist family of a little known village where the chimney of Alloy Steel Plant (Durgapur) now raises its head, Dr. Dutta qualified as an L.M.F. from the Campbel Medical School (now N.R.S. Medical College), Calcutta and joined Kulti Works Hospital in 1920. From an ordinary medical officer he rose to the post of medical officer in-charge and during his long 35 years of service he effected many improvements to the Hospital.

A man with an untiring zeal for social services Dr. Dutta made a deep impression in the minds of the Kulti people as President of East Bengal Refugee Relief Committee. He displayed outstanding courage during a railway accident in 1956 while coming from Calcutta, when ignoring his own injury he rendered relief to the injured passengers with the help of military personnel and saved many a life. Dr. Dutta rendered himself to the people of Kulti through manifold services to them. Besides being associated with the Kulti School and Kulti Sammilani, he took a leading part in establishing Kulti Chest Clinic under the auspices of Kulti Tuberculosis Association. He was President of the Association till his last days. A man of strong priniciple yet tender to the suffering humanity, Dr. Dutta had also a flair for writing. He depicted his view of life in a booklet entitled *Jivan Darshan* (Philosophy of Life).

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JOURNAL OF THE INDIAN MEDICAL ASSOCIATION

VOL. 64, No. 1 CALCUTTA JANUARY 1, 1975

State Medical Conference

XXXIX U. P. State Medical Conference Sitapur : 1974

The 39th Uttar Pradesh State Medical Conference was held at Sitapur amidst great enthusiasm Dr. K. P. Mehrotra presided over the conference which was inaugurated by Sri Lakshmi Shankar Yadav, Health Minister of U. P. The Scientific Session was inaugurated by Dr. G. P. Srivastava, Director of Medical & Health Services, U.P. A large number of delegates from all parts of U.P. attended the conference. The distinguished guests and the delegates were welcome by Dr. B. D. Kapur, Chairman of the Reception Committee. Dr. (Prof.) Nityananda Gupta presided over and conducted the scientific session on Hypertension. Several eminent teachers from Lucknow Medical College participated in the symposium. Dr Satyanand of Kanpur delivered the Dr. S P. Srivastava Oration. Dr. K C. Singhal, Organising Secretary, assisted by the members of the Reception Committee, office-bearers of Sitapur Branch and a group of devoted volunteers made excellent arrangements for the conference. The management and the staff of Sitapur Eye Hospital extended all cooperation in accommodating the delegates in the institution premises.

A number of important resolutions relating to the financial allocation for health care in the 5th Five-Year Plan, alarming drug situation, re-appearance of malaria and spread of small pox, insanitary conditions in the KABAL towns and cities in U.P., etc., was passed in the conference. Those who proposed or seconded the resolutions included Drs. M Prakash, R K. Seth, B. B. L. Dixit, K. L. Chopra, I. P. Gupta, R N. Gupta, M. S. Siddique, A. K. Tandon, B. R. Thukral, A L Shah, J. S. Vajpai, S. N Kapur, R. K. Seth, O. P. Goel, B K Kapur, Vineet Sharma, P. N. Tandon and A K. Gupta.

RESOLUTIONS

The following resolutions were passed in the conference :

1. The 39th U.P. State Medical Conference placed on record its deep sense of sorrow at the sad demise of the following members and offers its heartfelt condolence and sympathies to the members of the breaved families :—1. Dr. Achraj Jain (Aligarh), 2 Dr. Iqbal Mohammad (Bahraich); 3. Dr. Dauji Srivastava (Gorakhpur), 4. Dr. S. D. Banerji (Kanpur); 5 Dr. R. S Saxena (Kanpur); 6. Dr. Raj Kapoor (Kanpur), 7. Dr. R B. Saxena (Agra); 8. Dr. R. P. Dhawan (Bahraich); 9. Dr. Gulzari Lal Rohatgi (Kanpur); 10. Dr. Jawahar Lal Rohatgi (Kanpur); 11. Dr. Murari Lal Gupta (Rampur); 12. Dr. P. D. Kanchan (Shahjahanpur); 13. Dr. M. P. Mehrey (Sitapur); 14. Dr. Raman Nath (Varanasi); 15. Dr. L. N. Mathur (Varanasi), 16. Dr. R. P. Choudhary (Farrukhabad); 17. Dr. A. J. Faridi (Lucknow); 18. Dr. S. C. Chatterjee (Bareilly); 19. Dr. S. C. Chaurasia (Meerut); 20. Dr R. S Batra (Meerut), 21. Dr. V. R. Singh (Sultanpur) and 22 Dr S. C Chakravarty (Lucknow).

The conference also places on record its deep sense of sorrow at the sad demise of Smt. Sarla Mehrotra, wife of Dr. K. P. Mehrotra, President, I.M.A., U.P. State Branch.

2. The 39th U.P State Medical Conference is grateful to the President of India for appointing Dr. Chenna Reddy, a member of medical fraternity as the Governor of U.P This conference while welcoming him, offers its hearty felicitations and the profession its fullest co-operation to Sri Rajyapalji, in raising the standard of health of people of U.P. State and earnestly hopes that the problems of medical men shall be looked into sympathetically.

3. The 39th U P State Medical Conference views with great concern the food shortage and its distribution system in the country as it is affecting the health of the Nation due to malnutrition and undernourishment especially in children and mothers. The conference urges upon the Government to take suitable steps to provide adequate nourishment at least to the vulnerable section of the society.

4. This conference is alarmed at the shortage and extraordinary rise in the prices of common and life-saving drugs which has made the treatment of even common ailments very expensive. The conference urges the Government to take urgent steps so that the supply of common and life-saving drugs is made available to the public and the profession at a reasonable price.

5. This conference views with dismay and concern the draft 5th Five year Plan of U.P. which has ignored the recommendation of Central Council of Health to prepare the Plan of at least 10 per cent of the total outlay and has instead allocated a meagre share of 5.9 per cent without fixing any aims and objects. This meagre allocation will fail to meet the aspiration of the people and would further widen the gap of standards of medical care between those of All India level, other States and U.P. It further feels that 30 per cent economy cut in the matter of health care will further deteriorate the situation It urges upon the Government to reconsider it in its entirety

6 This conference urges upon the Government and the Medical Council of India to give new orientation to the medical curriculum as the present one does not serve the needs of the country effectively. This conference, therefore, suggests to the Government to adopt suitable modification to the curriculum and the training methods (keeping in view the recommendations of Medical Education Seminar of I M.A., held in Delhi in March, 1973

7 Whereas the U.P. State Government has replaced the uncoloured spirit with coloured denatured spirit, and whereas the State Government through a Press notification has advised against the use of coloured denatured spirit for sterilisation and surgical purposes ;

and whereas this notification has caused a scare among the doctors and patients against the use of coloured denatured spirit;

and whereas the use of rectified spirit for such purposes is practically out of question, because of its high cost and non-availability;

Be it resolved that this 39th U.P. State Medical Conference requests the U.P. State Government to issue necessary instructions for the supply of uncoloured denatured spirit or duty free rectified spirit to the hospitals, dispensaries and doctors for their professional use.

8. Whereas the use of certain drugs and injections result in allergic anayphylactic reactions which sometimes even prove fatal in spite of best precautions;

and whereas the lay public conversant with drug reaction lay the blame at the doors of the doctors;

and whereas the police and the officials treat the doctor as an ordinary criminal;

and whereas the doctor has to suffer loss of reputation and practice, manhandling, humiliation and prosecution in the Court of Law and incur expenses to defend himself.

Be it resolved that this 39th U.P State Medical Conference requests the U.P. State Government to issue necessary instructions that in the event of sudden and unusual death, the doctor should not be treated as an ordinary criminal, but the case should be referred to a Committee consisting of the Chief Medical Officer, President or Secretary of the Local Branch of the Indian Medical Association, a Professor of the Medical College wherever it exists or a senior local Private Practitioner for their assessment. If the Committee verdict is "*Not Guilty*", no further action need be taken, but if the Committee finds the doctor, Guilty", due process of law should be gone through.

9. The Conference is alarmed at the re-appearance of malaria and endemicity of smallpox in U.P. State. It urges upon the U.P. Government to take suitable steps to eradicate malaria and smallpox which is now localised only to this State.

10. This Conference views with serious concern that the state of sanitary conditions in the KABAL towns and cities of U.P. and urges the Government, Corporations, and the Municipalities that if the State is to be kept free of major epidemics, serious thought should be given to the problem.

11. This Conference once again demands that in view of the public dissatisfaction against the arrangements in the State and District Hospitals and Dispensaries and complaints against doctors, a Commission consisting of I.M.A., P.M.S., Medical College members should be appointed to go into the detailed working of hospitals and dispensaries and to suggest ways and means of improving the health care.

12 Whereas the general practice has now been accepted as a speciality, this conference urges upon the Government and the Universities to have a chair of general practice in the medical colleges in the State.

13 In view of the rapid advances in the medical science, this conference urges upon the Government and the Universities to arrange and help in the organisation of Refresher Courses both for in-service doctors, specialists and general practitioners to keep the medical men of the State uptodate in their knowledge.

14. In view of the special demands of the medical education to have uniformity of the standards, this conference is of the view that there should be a medical university in the State to which all the medical colleges should be attached.

15. Whereas the schools in U.P. collect a health cess from the students and whereas the school health service of the Government is now almost extinct, this conference urges upon the Health and Education Directorate of U.P. Government to look into the matters and utilise the funds so collected for the health care of the citizens of tomorrow.

XXIII M. P. State Medical Conference : Ujjain : 197

The 23rd Madhya Pradesh State Medical Conference was held at Ujjain on November 1-3, 1974 The first two days' sessions were held in the Humanities Block of Vikram University and the third day's session at Nagda at the Club-Hall of Birlagram (Gwalior Rayons).

The inaugural session started on 2nd November at the Vikram Kirti Mandir of Vikram University with Saraswati Vandana programme organised by Dr. C. S Yadav. Dr. R. S. Shukla, Chairman of the Reception Committee, welcomed the distinguished guests and the delegates. Following this messages received from the President, Vice-President and Prime Minister of India, the Governor, Chief Minister, Health Minister and Director of Health Services of Madhya Pradesh and the Vice-Chancellor of Vikram University were read by the Organising Secretary, Dr. O. P. Bhargava. The inaugural address was delivered by Kumari Vimla Verma, the State's Health Minister. In her address, Kumari Verma stressed the need for Government and private doctors working in close co-operation for the benefit of the people and assured the doctors in Health Service of her Government's due consideration of their various grievances. Dr. R. K Mishra delivered his Presidential address in course of which he dwelt on the various medical and health problems confronting the profession. The Hony Secretary of M. P. State Branch presented in brief the annual report of the State Branch. Dr. Suman also briefly addressed the gathering. The function concluded with the singing of Jana Gana Mana in which the audience also participated.

The scientific session started under the chairmanship of Dr. D. Singh, The main feature of the first sitting was a talk by Dr. Sepaha, who spoke on Magnesium in Heart Diseases. Later Dr. R. K. Mishra announced that Dr. R. S. Shukla would donate Dr B. C. Roy Oration Gold Medal for 1975-76 in the name of his father, Sri R. D. Shukla.

In the second sitting held under the chairmanship of Dr. Akbar Ali, the following papers were presented: Dr. N. L. Bordia on Use and Abuse of Reserve Drugs; Dr. N. P. Mishra on Diagnosis of Renal Failure; Dr. S. R. Jain on Problems Encountered in E.C.G. Diagnosis of Ischaemic Heart Diseases, Dr. B. Singh on E.C.G.—Tread Mill Test; Dr. I. B. Goel on Social Ophthalmology; Dr. N. K. Mahadik on a Trial of Trimethoprim and Sulpha Methoxazole in Clinically Diagnosed Whooping Cough. The presentation of papers was followed by a panel discussion on Hypertension in which about 14 doctors participated including Dr. D. Singh, Dr. Sepaha, Dr. Bhagwat, Dr. Pathak and Dr. Mathur. Padma Bhushuan, Dr. S. K. Mukerjee, who was the Chairman on this occasion, summarised the whole discussion.

Besides, the scientific session a social gathering was arranged when the local delegates along with some elites of the town met the delegates from other parts of the State. Dr. S. K. Mukerjee was present on this occasion along with Sri B. K. Seth and Sri Rathi A dinner was hosted by the local Chemists

Association to the accompainment of Police Band in the hall of the Humanities Block. This was followed by a variety entertainment programme presented by Dr. Yadav and his team.

On 3rd November the delegates were taken to Nagda by bus, where the third day's session was held. The day's programme was devoted mainly to scientific sessions. In the first sitting held under the chairmanship of Dr. Nigam the following members presented papers: Dr. Nagrath—Intestinal Obstruction-Diagnosis and Management; Dr. (Mrs.) Nagrath—Congenital Anomalies of the Female Genital Tract-Diagnosis and Management; Dr. M. V. Kamath—A New Look at Surgery of the Inguino-Scrotal Region, Dr. Usman—Retroperitoneal Tumors; Dr. Taneja—Rumalaya in Osteoarthritis; Dr. G. N. Sharma—Intra-Muscular Myxoema of Deltoid; Dr. Sachdev—Experiences with Healex Spray; Dr. K. C. Khare—Romances in Dermatology. An interesting lecture was delivered by Dr. R. D. Lele on Recent Advances in Nuclear Medicine. The session concluded with a vote of thanks proposed by Dr. K. D. Pathak, Vice-Chairman of the Organising Committee.

XXXIV The Bihar State Medical Conference: Purnea: 1974

The 34th Bihar State Medical Conference was held at Purnea on November 16-18, 1974 in the campus of the Station Club, Purnea. The conference commenced on 17th November morning when Dr. L. P. Choudhry, President, I.M.A. Bihar State Branch, unfurled the I.M.A. flag. The inaugural function was held in the spacious pandal erected in the Station Club campus. Dr. G. S. P. Sinha, Chairman of the Reception Committee, welcomed the delegates and the guests. Shree Lahtan Choudhury, Health Minister, Bihar, inaugurated the conference. In course of his address he appealed to the doctors to take up service in the rural areas and dedicate themselves fully to the services of the ailing humanity. He said that it was not possible for the Government because of financial difficulties to meet all their demands. Government was nevertheless sympathetic to their grievances, he said. Dr. Jyotirmoy Majumder, President-elect, I.M.A., who was present as the Chief Guest, said that mere appreciation of their work would not inspire the doctors to remain dedicated to the service of the people. The doctors expected the Government to appreciate that they were working under numerous odds and that they had genuine grievances which required to be removed. He assured the Government that medical profession was prepared to make necessary sacrifice for their countrymen, but identical gesture should also be shown by officials from other wings of the Government Dr. A. K. N. Sinha, a past-President of I.M.A. and President-elect of Commonwealth Medical Association, referred to the large number of Indian doctors abroad who were inclined to come back to their motherland provided they got the right opportunity to serve the people. Speaking of Government's call to dectors to move to the rural areas, he said according to Government's own statement the income of 50 per cent of the population was only 75 paisa. He did not know how the doctors would come to the help of these rural people who could hardly afford the luxury of treatment. He urged the Government to reorient its thinking about rural health care and stressed the need for providing adequate quantities of drugs, equipment, etc., to enable the medical profession to serve the people better. Dr. Sinha expressed the view that nationalisation of health services was the only solution under the prevailing conditions of the country for the problem of organising better rural health care. Dr. Dinabandhu Banerjee, President-elect, Bengal State Branch of I.M.A. said that many problems connected with the public health and particularly rural health could be solved through the spread of health education. He narrated in this connection his own experiences with the Health and Hygiene Councils formed in certain areas of West Bengal at the village level, which were doing commendable work in the field of health education and immunisation programmes. Paying his tribute to the contribution of Bihar State Branch to the rural health programmes of the I.M.A., he said that Bengal and other State Branches of I.M.A. were highly impressed by what the Bihar State Branch had done both for the cause of I.M.A. and for the betterment of public health through observance of health week, school health examination and tubewell movement.

The outgoing President, Dr. L. P. Choudhry, formally installed Dr. R. P. Okhandiar of Bhagalpur as President for the year 1974-75. Following this Dr Okhandiar delivered his Presidential address. The scientific session was inaugurated by Dr. A. K. N Sinha. In course of his address Dr. Sinha stressed the need for providing proper facilities for scientific research which was almost negligible in this State. He also pleaded for imparting better training to the students in different medical colleges as they would be the doctors of to-morrow and wanted reduction in the number of admission to the medical colleges which were not properly equipped. The scientific session had two sittings devoted to discussion of surgical and medical topics. The first sitting was presided over by Dr. U. N. Shahi, an eminent surgeon and the following speakers besides U. N. Shahi who spoke on Hepatic Lobectomy delivered lectures: Dr. Motilal Singh on Urinary Obstruction, Dr. A. A. Hai on Use of Autogenous Vein Graft, Dr. R. Thakur on Gastrjejune Colic Fistula and Dr. A. M. Chatterjee on Septicaemia. In the second sitting there was a panel discussion on Ischaemic Heart Disease in which the participants were Dr. C. P. Thakur, Dr. S. N. Arya, Prof. A. Saran, Dr. S. M. Rahman, Dr. S. N. Verma, Dr. A. Prasad and Dr. S. Abedin. Dr. A. K. N. Sinha, who was Chairman of this session, acted as the moderator. In their discussion the speakers emphasised the preventive aspect of Coronary Artery Disease and also dealt with its rapidly developing surgical treatment.

PRESIDENTIAL ADDRESS

At the outset Dr. R. P. Okhandiar referred to the two significant achievements for the State Branch—the election of Dr. A. K. N. Sinha, a past President of I.M.A. from Bihar as President of Commonwealth Medical Association and consolidation of the doctors in the Health Service of Bihar. Dr. Okhandiar said that while each and every President of Bihar IMA had advised the State Government to meet the just demands of the doctors in health service, it was deplorable that except for partially conceding a few demands concerning the service conditions of block medical officers and promotion of sub-assistant surgeons to civil assistant surgeons cadre, the State Health Department had done little for the service doctors. It is the intransigence of the State's health authorities that forced 2300 out of 2500 service doctors to tender mass resignation. He made it clear that the I.M.A. stood for all-out support to the charter of demands of the service doctors and he believed that with the formation of a Joint Action Committee by Health Service Association and I.M.A the movement had gained new strength. Urging the people to realise the justification of the struggle of the service doctors, he pointed out that it was impossible for the doctors to serve the people if there was a non-existent medical service and there was no medicine, no bandage, not enough beds or diet. He appealed to the Health Minister to join hands with I.MA. in creating a public opinion in favour of proper Medical Service and to improve the health care in the State by providing well-equipped hospitals, enough medicines for all, and an allowance of Rs. 200/- to rural medical officers as incentive for their hard work and secluded life with compensating allowance for the education of their children. Dr. Okhandiar also demanded justice for the paramedical staff as also the non-medical personnel employed in the Health Department many of whom have to remain temporary in spite of long years of service.

Referring to the unutilised potentiality of a large number of private practitioners in the country, Dr. Okhandiar deplored that no medical manpower survey was undertaken to ascertain their exast number either in this State or in the whole country, and that even the valuable document prepared by the I.M.A. about 5-7 years ago containing a report of survey undertaken by the Bihar State Branch of IMA still awaited the favour of the Government's financial help for publication. He expressed his surprise that Government did not seek the help of private practitioners in its eradication programmes for smallpox or other communicable diseases while there were numerous instances of successful cholera inoculation and smallpox vaccination programmes conducted by them at various places in Bihar during the health week observed by I.M.A. He urged the Government to requisition the service of private practitioners in all possible spheres of health service including rural health centres where Government could persuade them to settle down after providing some financial assistance.

Dr. Okhandiar strongly pleaded for paying living wages to young medical graduates so that they could work in the hospitals without having too worry for their maintenance. He suggested that their training period should be fully rationalised and some of them should be given facilities for postgraduate specialisation depending upon their academic career, aptitude and performance during the training period. He stressed the need for providing immediate employment to the young graduates and absorbing some of them in the rural centres on part-time basis. Dr. Okhandiar deplored the disarray of the medical education in Bihar and pleaded for streamlining of the same through the creation of a medical university having full control over all medical colleges in Bihar, setting up an independent directorate for medical education and separation of the teaching cadre from general health services cadre. Referring to the private medical colleges which were imparting sub-standard medical education he pleaded for Government's assistance to such institution in the form of functioning hospitals so that they could fulfil the required standard of the Medical Council of India. He also urged the Government to compensate these colleges with suitable subsidies so that the charging of enormous capitation fees by these colleges could stop.

Expressing grave anxiety at the non-availability of drugs leading to black-marketing in the same and the growing menace of spurious drugs, he asserted that the only answer to these evils was nationalisation of drug industry at the production level. At the distribution level he suggested formation of drug co-operatives and requested doctors to explore the possibility of such cooperatives in their own locality. Speaking of the doctor-public relationship he granted that in spite of high ethical standard and moral obligations maintained by the majority of the profession some members succumbed to the pressure of corrupt practices and nepotism prevailing in the country. But there were instances of human failure which were often exaggerated by the press as delinquency on the part of doctors, while instances of their silent sacrifice and devotion did not receive any publicity. He pointed out that in Bihar doctors have never failed to join relief activities on a large scale on occasions of natural calamities and recently they have rendered commendable service in the flood-affected areas of North Bihar and among the suffering people from Bangladesh. He urged the members to improve the image of the profession and go nearer to the people by actively participating in the public health programmes of I.M.A.

Staying Charges for Guest Rooms at IMA House New Delhi

In course of a circular dated December 13, 1974 addressed to the Hony. Secretaries of all State/Territorial and Local Branches of I.M.A., Dr. P. C. Bhatla Hony. General Secretary, I.M.A. states:

The Working Committee at its meeting held at New Delhi on September 15 and 16, 1974, reviewed the above and revised the staying charges payable by the members of the Association and their families at the I.M.A. House, New Delhi, in view of the rising cost as under:

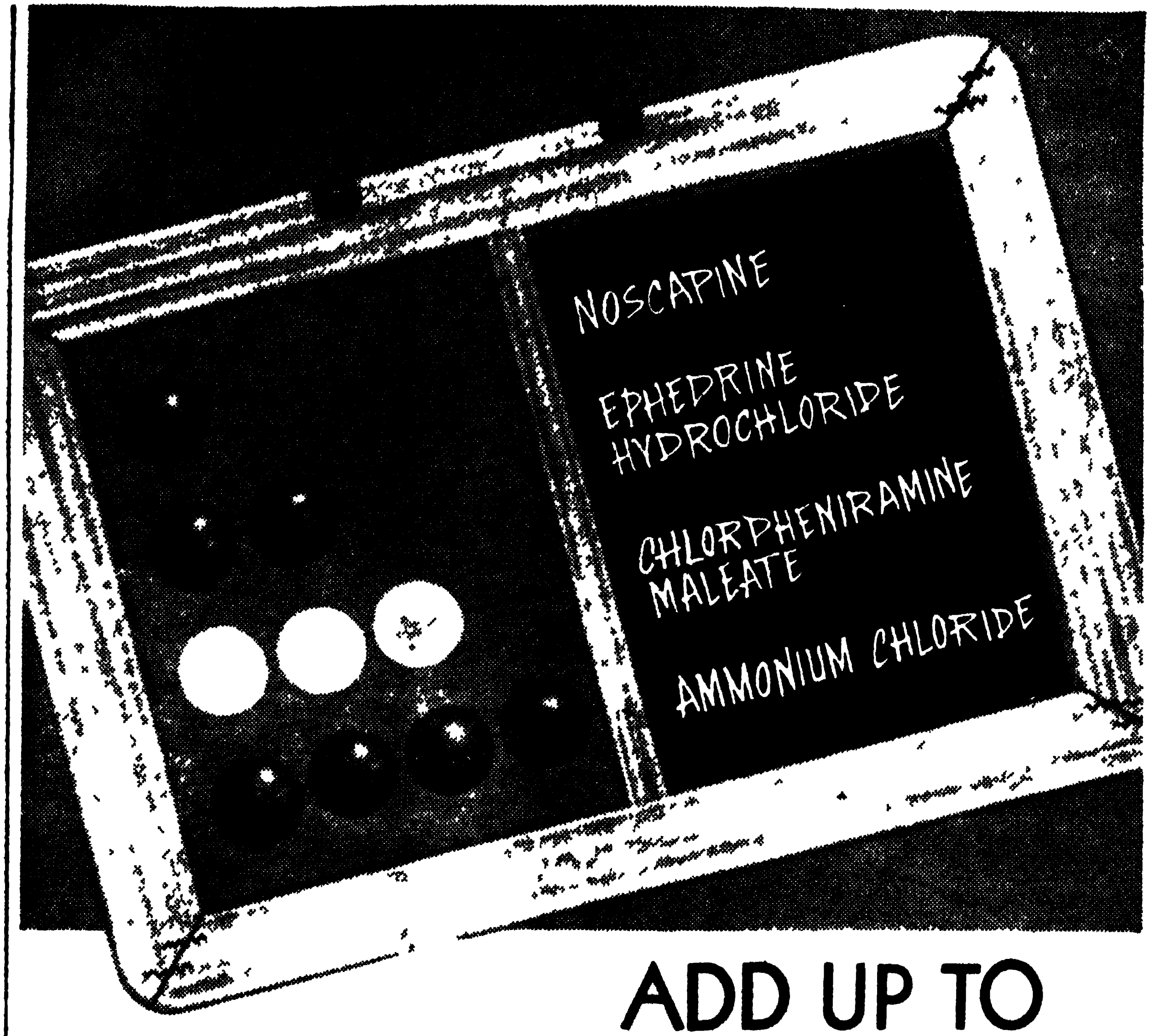
	Old Charges	Revised Charges
Non Air-conditioned Room	Rs. 10/-	Rs. 12.50 per day
Air-conditioned Room	Rs. 20/-	Rs. 25.00 per day

With corresponding increase in case of children on the schedule fixed earlier.

These charges will come into force with effect from February 1, 1975. This may be brought to the notice of the members.

XV Andhra Pradesh State Medical Conference : : Khammam : : 1975

The 15th Andhra Pradesh State Medical Conference will be held at Khammam on January 10-12 1975. The conference will be presided over by Dr. C. Vyaghreswarudu, President, A.P. State Branch for 1974-75. Dr. A. K. N. Sinha, past President of IMA, has been invited to address the inaugural session Dr. N. R. Swamy, Director of Medical Services, A.P., is expected to open the scientific session. Dr. C. Raja Ramamohan Reddy of Vizag will deliver the Dr. Y. S. Rao Memorial Oration. Members of IMA in Andhra Pradesh have been cordially invited by Dr. N. Appa Rao, Organising Secretary, XV A. P. State Medical Conference, Khammam.



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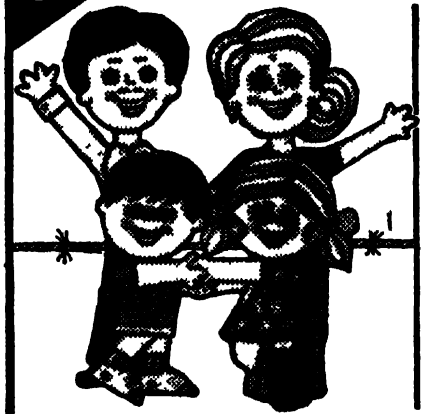

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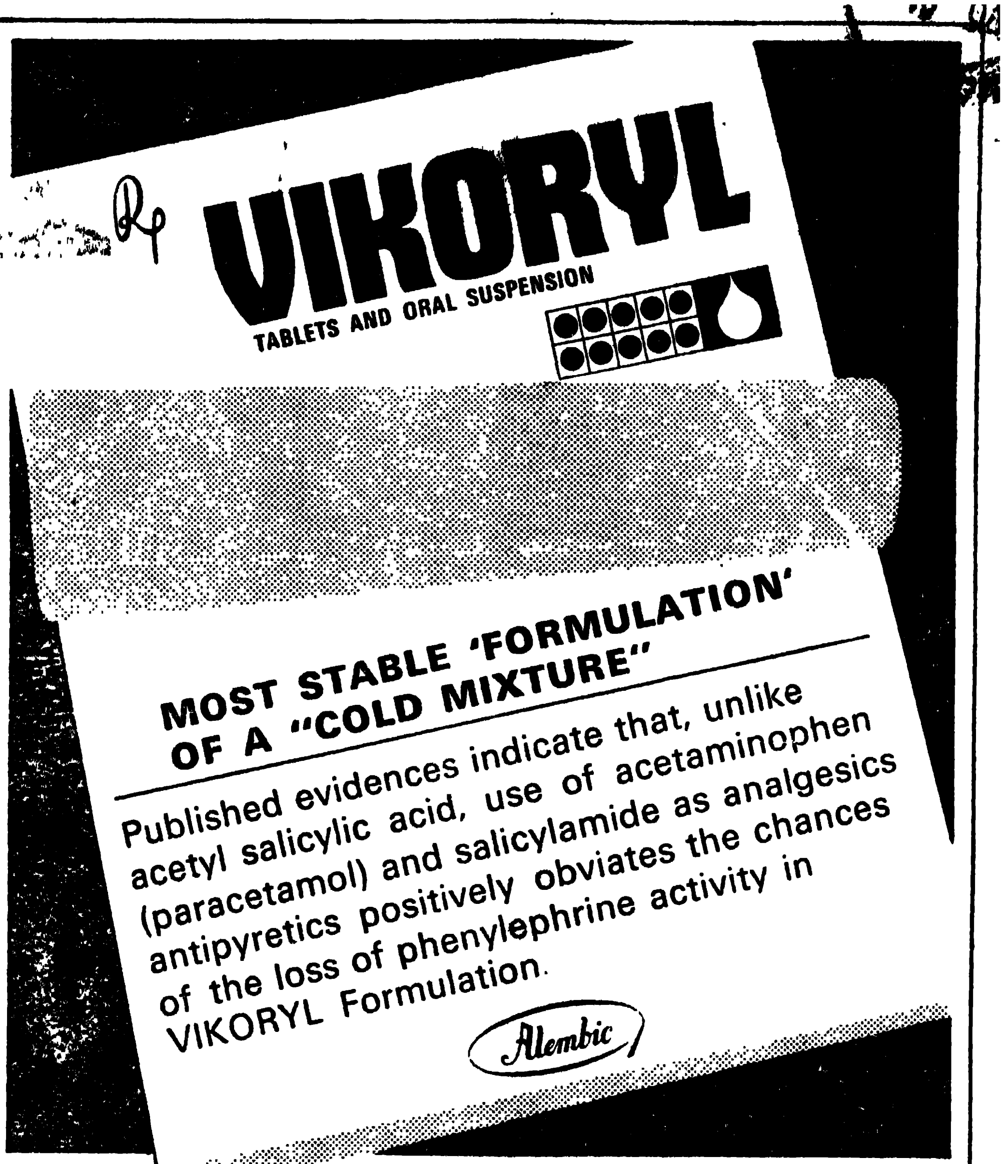
and published by him on behalf of the Indian Medical Association from 53, Creek Row, Calcutta 700
Editor—Dr. A. B. Mukerjee, M.D. (Cal.), F.R.C.P. (Lond.).



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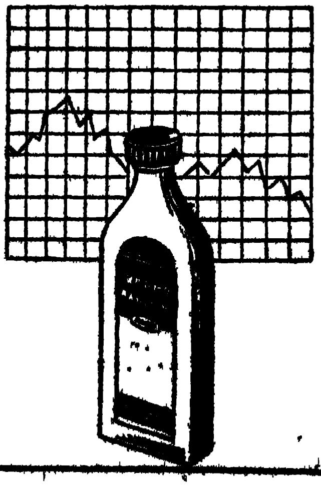

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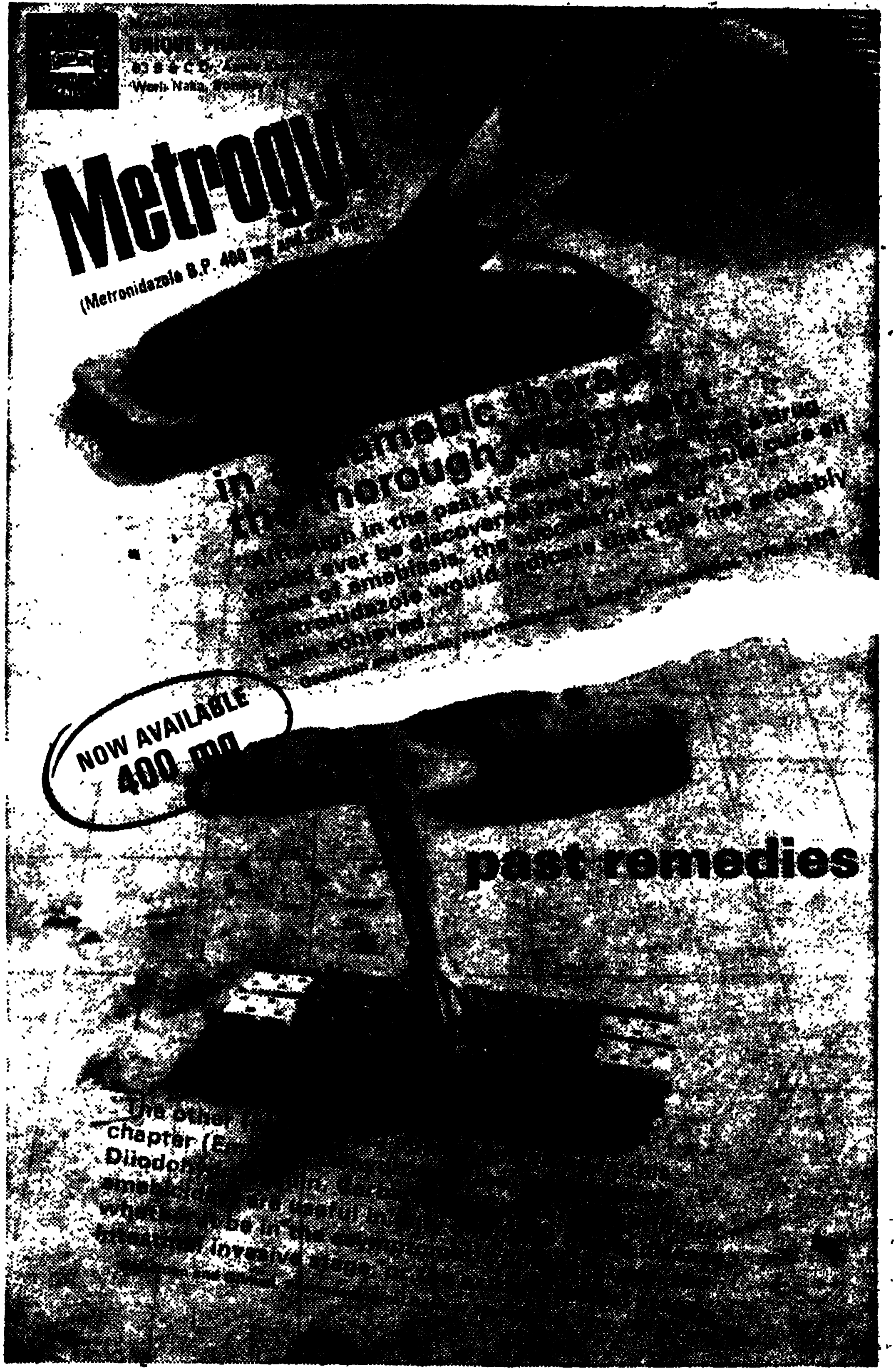
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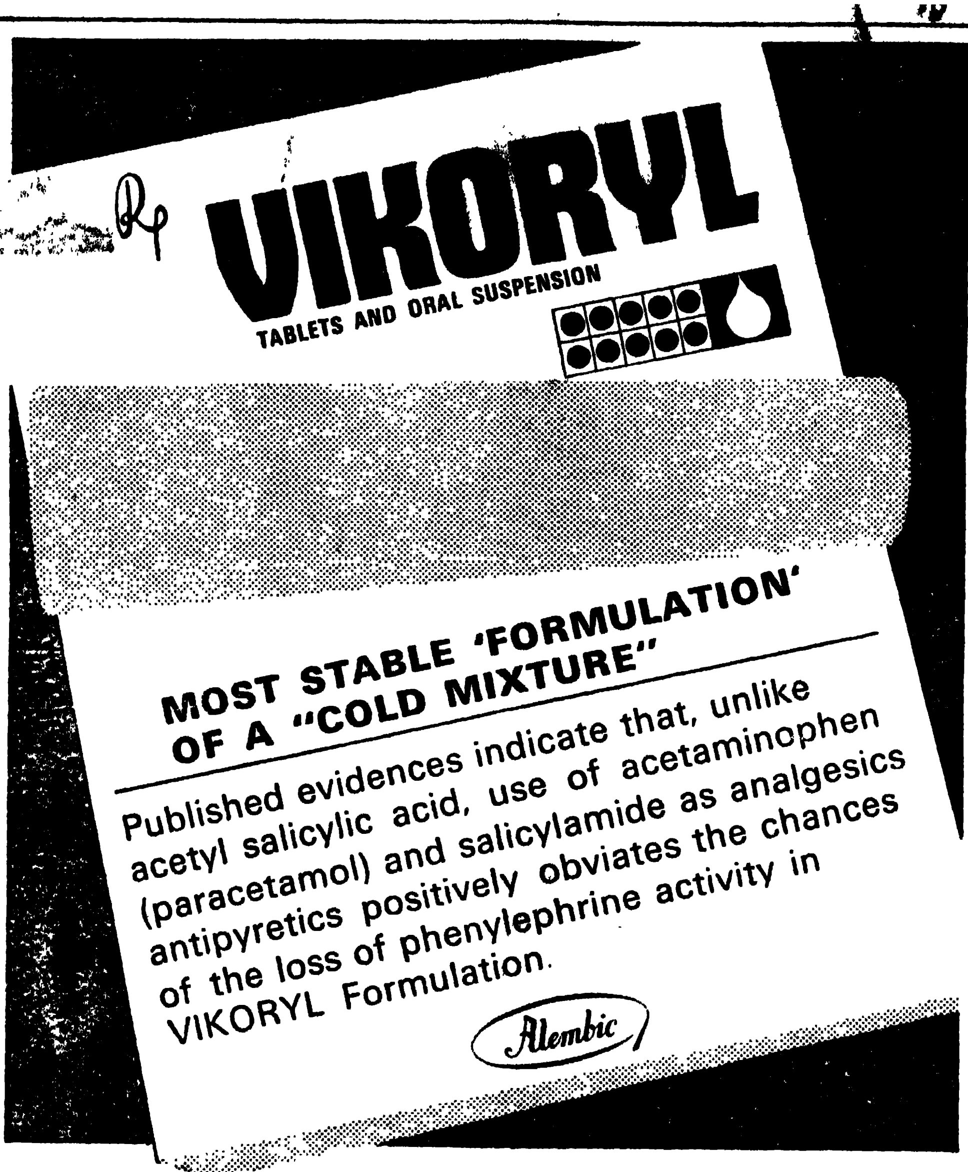

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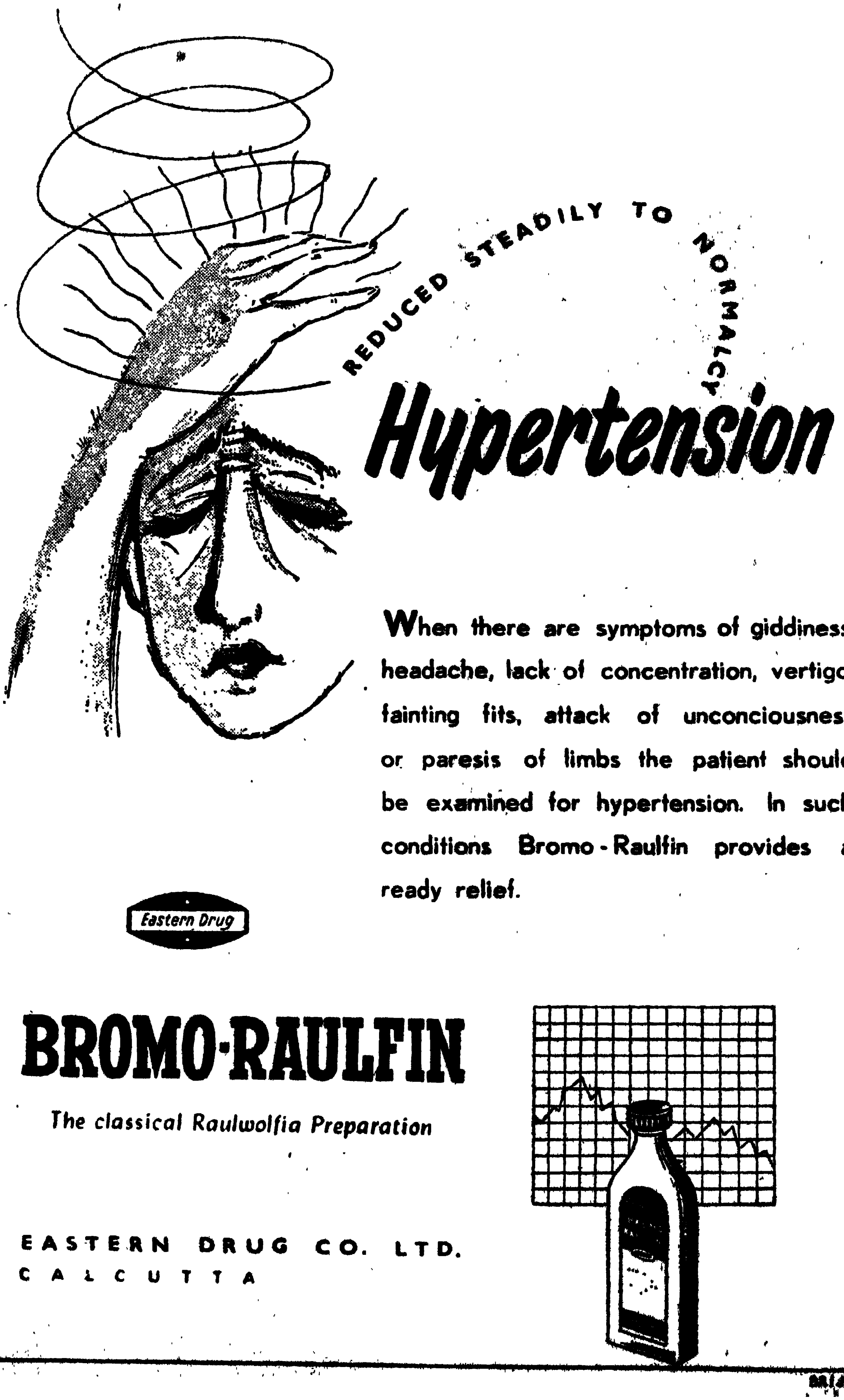

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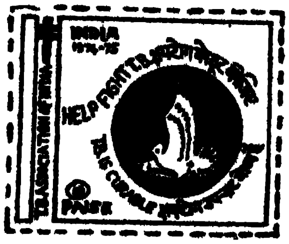

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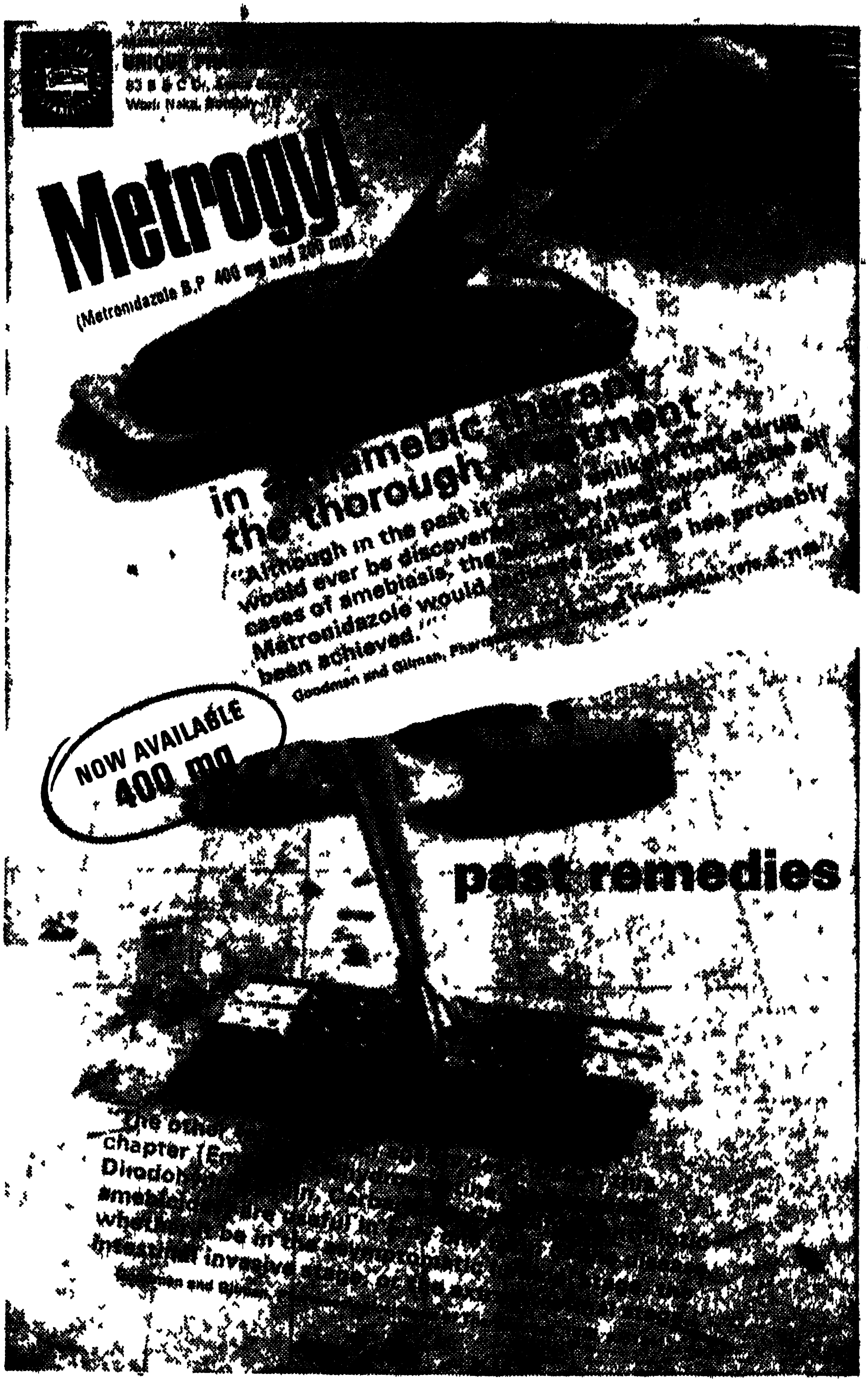
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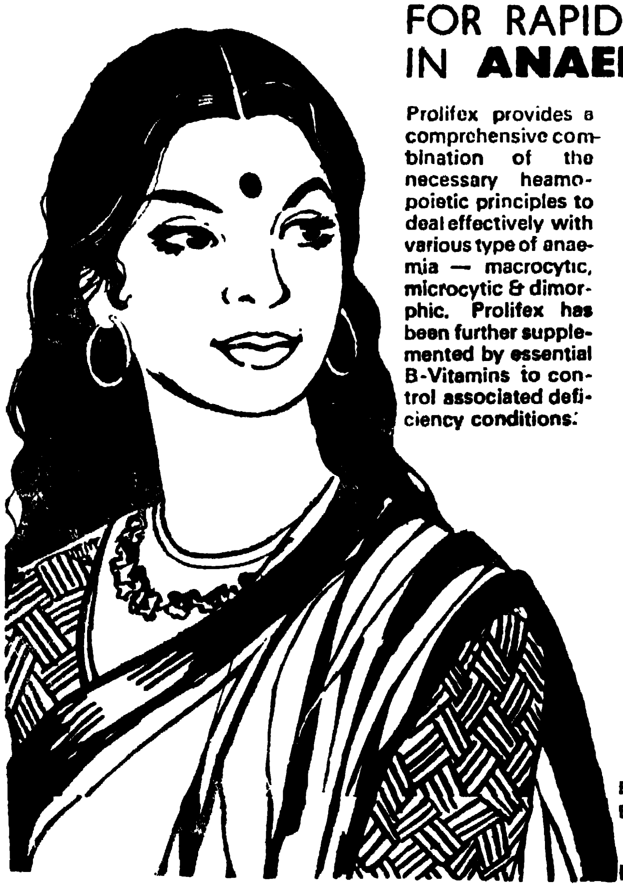
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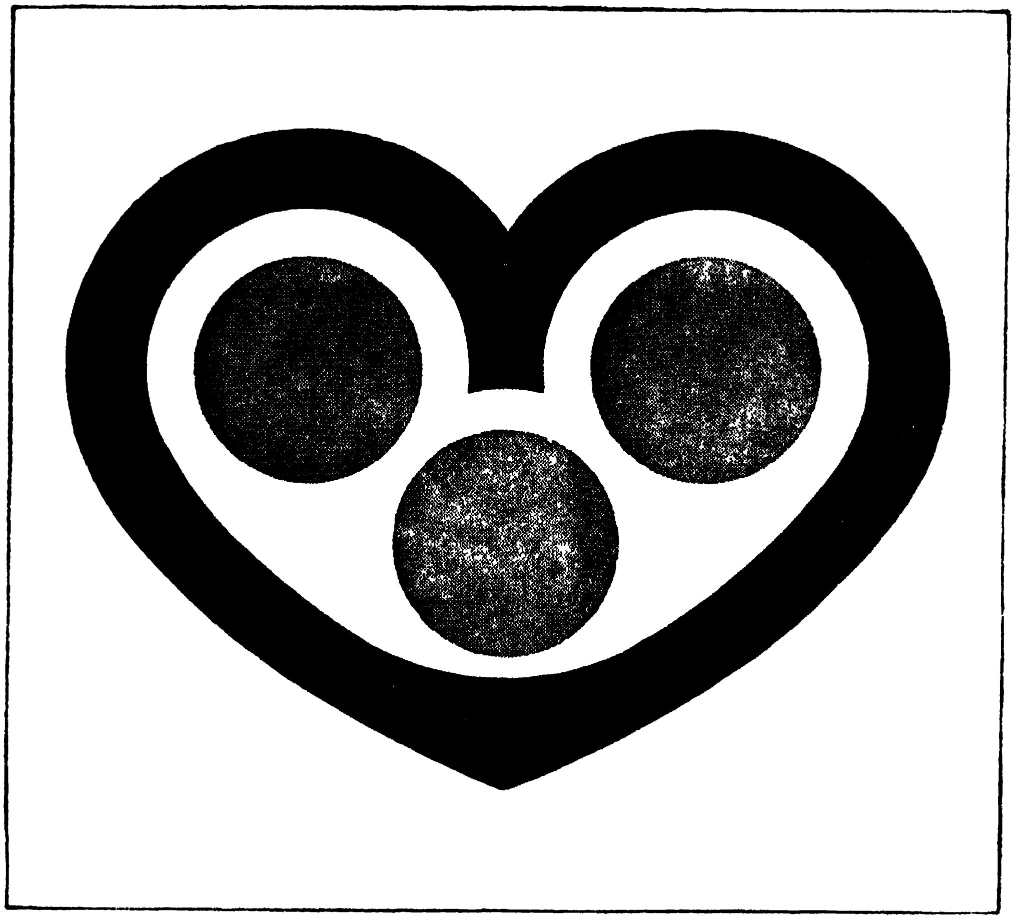

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Journal of the
Indian Medical Association

VOLUME 64
NUMBER 2

PUBLISHED TWICE A MONTH
EDITOR—A. B. MUKERJEE, M.D. (CAL.), F.R.C.P. (LOND.)

CALCUTTA
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ORIGINALS AND PAPERS

1

Methods of Intestinal Anastomosis—An Experimental Study in Dogs

A. N. SINHA*, R. C. ARANYA**
R. G. GOEL***, K. S. MEHDIRATTA****

[Received for publication August 9, 1973]

Since the vedic period attempts have been made to suture the intestine by various methods. Charaka, Susruta and Vagbhata sutured the intestine using ant-heads as suture material (Major, 1954). Since 1826, Lembert's seromuscular suture became the basis of the conventional 2-layer inverting anastomosis which is, however, associated with a high degree of leakage, obstruction of the lumen, delayed intestinal motility and is time consuming (Hargreaves and Keddie, 1968). Quicker methods of single layer anastomosis have been suggested. The aim of the present study was to evaluate 2 such methods for their safety for clinical practice and to study the method of healing after each type of anastomosis. The methods tried were : (a) Sleeve method; and (b) end-on method.

MATERIAL AND METHOD

Twenty-four healthy mongrel dogs, 12 female and 12 male, weighing from 9 to 15 kg. were used in this study. The bowel was prepared with an anthelmintic agent against tapeworms, 10 days prior to operation. The animals were anaesthetised by injection of pentobarbital sodium, 15 mg./kg. body weight preceded by injection of morphine and atropine as pre-medication; intravenous fluids were given during the operation.

The abdomen was opened with a right paramedian transrectal incision. Anastomosis was done in the following manner in the 2 groups.

Sleeve method—The distal end of the ileum was invaginated into the proximal one for about 2 cm. by 2 or 3 through and through interrupted stitches. One of these stitches was put at the mesenteric border. This was followed by continuous Lembert's seromuscular stitches in between the edge of the proximal and seromuscular coat of the distal loop around the anastomotic line.

End-on method—The 2 ends of the ileum were anastomosed by interrupted through and through linen stitches (3—5 mm. apart) starting from the mesenteric border. The sutures were tied tightly so that the soft tissues were cut through and included only the collagen tissue in the submucosa.

The animals were sacrificed at intervals ranging from 1 to 6 weeks. The anastomotic area was dissected out. Any adhesion, fibrosis, scarring in the anastomotic area, patency of the lumen, proximal dilatation, if any, were observed and recorded.

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Microscopic sections from the site of the anastomosis were taken and studied.

In case of death of the animal, an autopsy was done to find out the cause of death and the site of anastomosis was taken for histopathological examination.

OBSERVATIONS

Out of 24 dogs which were operated, 9 dogs died, 4 with sleeve resection, 3 with end-on and 1 each due to bleeding disorder and anaesthetic shock.

Sleeve method—Thirteen dogs were operated and 4 dogs died from the 2nd to 4th postoperative days. On autopsy 2 deaths were due to leak at mesenteric border, 1 at the antimesenteric border and 1 due to anastomotic narrowing.

End-on method—Nine dogs were operated and 3 died on the 2nd to 5th postoperative days, 2 due to leak at mesenteric and 1 at the antimesenteric border.

Presence of plenty of adhesion was the most prominent feature in the autopsy finding. Slight proximal dilatation was detected in all the sleeve method but in the end-on it was absent.

Histological observations—The most striking feature of the sleeve method in the early stage (1 week) was patchy necrosis of the mucosa, muscle and serosa of the invaginated portion of the distal loop with formation of micro-abscesses. In no instance was continuity established between the muscle coats of the 2 ends of the anastomosis. Regeneration of the mucosa was sluggish and even after 6 weeks was limited to an almost insignificant ingrowth of single layer epithelium (Fig. 1).

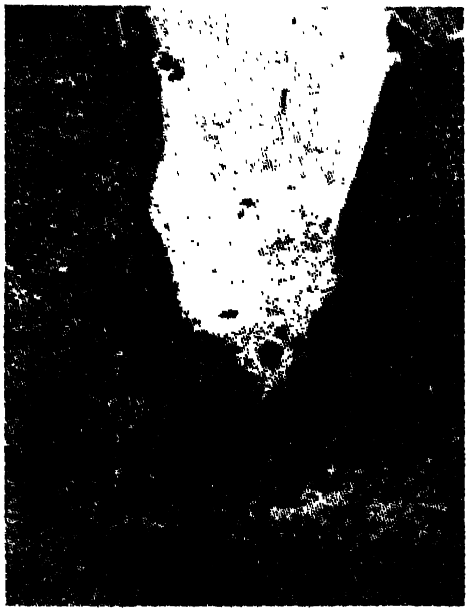

FIG. 1—SHOWING PHOTOMICROGRAPH WITH SLUGGISH REGENERATION OF THE MUCOSA AFTER ANASTOMOSIS BY THE SLEEVE METHOD

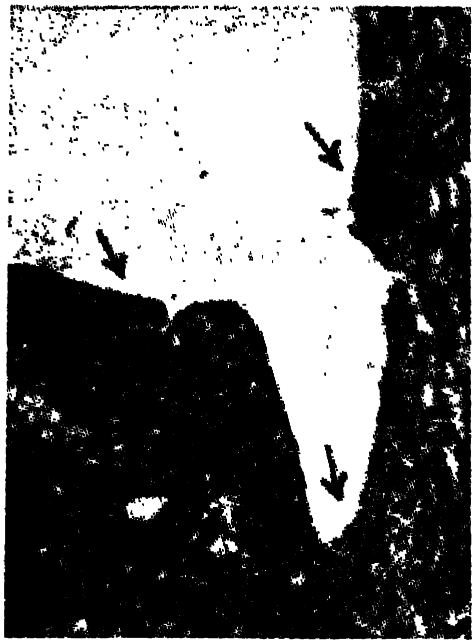

FIG. 2—SHOWING PHOTOMICROGRAPH WITH COMPLETE MUCOSAL REGENERATION AFTER ANASTOMOSIS BY THE END-ON METHOD

The microscopic study of the end-on variety revealed a superior anatomic alignment, i.e., there was union of serosa-to-serosa, muscularis-to-muscularis and mucosa-to-mucosa. Although islands of fibrous tissue were found at the site of anastomosis, there was an attempt at healing by primary intention. There was complete mucosal regeneration at the anastomotic site even at the end of the 1st week (Fig. 2).

DISCUSSION

The standard 2-layer inverting anastomosis which is still the basis of intestinal surgery in most of the centres since 1826, has many drawbacks like tissue necrosis, microscopic abscess formation (Buchin and Van Geertruyden, 1960), leakage and obstruction.

Hamilton (1967) has gone to the extent of saying that the double-row inversion in the standard method, generally giving it greater security, is probably the very factor which, by jeopardizing arterial supply, venous and lymphatic return, renders it more prone to vascular necrosis and infection. So 1-layer anastomosis has been repeatedly tried both experimentally and clinically by various authors recently including Buchin and Van Geertruyden (*loc. cit.*), Heifetz (1964, 1966), Jourdan (1966), Gambee *et al.* (1956), Beling (1957) with encouraging results.

Telescopically invaginated bowel wall in sleeve method, a sort of double breasting effect, was thought to strengthen the anastomosis and afford a guarantee against leak, but contrary to the expectation there was a high mortality of 30.7 per cent (4 out of 13 dogs). Hargreaves and Keddie (*loc. cit.*), however, had 50 per cent mortality on similar experiments.

The overall picture of the sleeve variety as revealed by the histological observation is not encouraging. This is consistent with the findings of Garner *et al.* (1969). It proved disappointing due to complete necrosis of mucosa, and patchy necorsis of muscle and serosa of the invaginated portion of distal sleeve even at the end of 1st week. The necrosis, infection and abscess formation and healing by secondary intention practically spoiled the double breasting effect and led to the weakening of the anastomotic strength.

End-on reconstitution is thought to be superior to classic inversion or eversion of the bowel wall, as when the soft tissues are severed by sutures, pressure on the microcirculation is released and results in minimal ischaemia. This unorthodox manoeuvre, however, cuts through all the layers except the collageneous fibres in the submucosa which form the basis of approximation of the bowel ends.

In our experiments, 3 out of 9 dogs died, a majority due to leak at the mesenteric border in the beginning of the series. Initially we started the anastomosis from the anti-mesenteric border and completed at the mesenteric border where poor visibility and mechanical difficulty of placing the suture were probably responsible for the failures. In later experiments we started the anastomosis from the mesenteric border and finished at the anti-mesenteric border and we did not have any death in the last 5 dogs.

Histological appearance in end-on variety also proves the superiority of the technique as evidenced by complete anatomic alignment, healing by first intention and mucosal regeneration at the anastomotic site even at the end of the 1st week.

SUMMARY

Two new methods of single-layer intestinal anastomosis were tried in dogs, i.e., end-on and sleeve methods. In the sleeve method there was a high mortality (4 out of 13 dogs) due to leak and anastomotic narrowing. Histological appearance showed incomplete healing by secondary intention. End-on method, if done with proper precaution, appears to be a better procedure due to sound microscopic healing by first intention and lesser complications, e.g., leak, anastomotic narrowing, proximal dilatation, etc. While the results of the end-on method have an edge over the sleeve method, whether either of them can replace the universally employed conventional 2-layer inverting technique remains to be proved.

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2

Coagulation Profile of Congenital Heart Disease during Cardio-Pulmonary Bypass Surgery

DILIP K. BHATTACHARYA*, R. L. SAHA**
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SAIBAL GUPTA*****

[Received for publication December 9, 1973]

Open heart surgery using extracorporeal circulation produces haemostatic defects which, if severe enough, causes abnormal postoperative bleeding (Hardisty and Ingram, 1965). In recent years improvement of the techniques of extracorporeal circulation has considerably reduced the

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severity of haemostatic derangement to a safe level in ordinary clinical perfusions, but it is still significant in certain types of heart diseases, such as cyanotic congenital heart diseases, where latent haemostatic defects become manifest during bypass surgery (Paul *et al.*, 1961; Bloom, 1963; Philips *et al.*, 1963). In the present paper some factors of haemostatic mechanism in congenital heart diseases undergoing bypass surgery have been presented in order to evaluate such changes and to evolve a routine therapeutic schedule for the effective control of post-bypass bleeding.

Material and Method

The study was conducted on a random series of 18 cases of cardio-pulmonary bypass surgery using extracorporeal circulation by the Blood Bank of the Nilratan Sircar Medical College and Hospital, Calcutta, during 1971-1972. Only those patients on whom complete laboratory data were available were included in the present series and the patients were grouped according to the following criteria :

Group I. Congenital heart diseases without cyanosis and short bypass time (<45 minutes)

Atrial septal defect	8 cases
Ventricular septal defect	1 case
Pulmonary stenosis with ASD and anomalous pulmonary venous drainage	1 case
Valvular and infundibular pulmonary stenosis	1 case

Group II. Congenital heart diseases with variable degree of cyanosis or polycythaemia and prolonged bypass time (>45 minutes)

Atrial septal defect with pulmonary stenosis	2 cases
Fallot's tetralogy	2 cases
Fallot's tetralogy with unilateral pulmonary stenosis	1 case
Double outlet right ventricle with pulmonary, infundibular and valvular stenosis	2 cases

The patients were operated upon with a Rygg Kyvsgaard heart lung machine using Rygg-Kyvsgaard disposable bubble type plastic bag oxygenators* and the bypass was routinely conducted at normothermia using high flow rate. The bypass time ranged from 22 minutes to 87 minutes.

Haemodilution to the extent of 30ml./kg. body weight was obtained using 5 per cent dextrose solution balanced with sodium bicarbonate (2ml./kg. of 7.5 per cent solution), Ringer-lactate (3ml./kg.), potassium chloride (1 mEq./kg.) and a small amount of mannitol. Blood was added to the priming fluid only when the patients were too young or very anaemic. Heparinisation of blood, postoperative neutralisation of heparin and haemostasis were done as per following schedules.

A. The total dose of heparin was calculated as follows : 3mg./100ml. of calculated blood volume of the patient; 3mg./kg. body weight administered during operation and 5mg./100ml. of the priming fluid or any other transfused fluid. Blood for the bypass surgery was collected on the day of operation in ACD bottles*.

B. Post-bypass neutralisation of heparin was done by titration of post-bypass samples with serially diluted protamine sulphate, and the least quantity of protamine sulphate that corrected the clotting time of blood samples to 5 minutes was noted. The total neutralising dose of protamine sulphate was calculated by multiplying the quantity of protamine per ml. of blood used for correcting the clotting time by the total blood volume at the time of operation (Bhattacharya and Gupta, 1973).

C. An antifibrinolytic agent (6-aminocaproic acid†), 2-4 g. in the post-bypass period depending on fibrinolytic activity of the post-bypass plasma samples was used.

D. Stored blood (less than 48 hours) was used in the ratio of 250ml. of fresh blood for every 500ml. of stored blood to promote haemostasis or to correct blood loss.

In the week preceding bypass surgery, screening tests for any haemostatic defect were carried out essentially after Dacie and Lewis (1968) unless otherwise mentioned. Platelet count was done, bleeding time, clotting time, prothrombin time, partial thromboplastin time, fibrinogen and fibrinolysis time were estimated and thromboplastin generation test was carried out before and after bypass surgery and during subsequent follow up.

Fibrin monomer was screened by serial dilution protamine sulphate test (SDPS test) after Gurewich and Hutchinson (1971) and compared with the preoperative samples and control plasma as reported briefly by Saha and Bhattacharya (1973). Blood haemoglobin, packed cell volume, plasma haemoglobin and serum bilirubin were estimated in pre- and post-bypass samples to assess haemolysis. Postoperative bleeding was assessed by measuring the volume of thoracotomy drainage.

Results

An earlier communication states that the degree of haemostatic defect is related to the duration of bypass in open heart surgery (Bhattacharya *et al.*, 1973). Therefore, for the purpose of evaluation of cases such factors as duration of bypass and the volume of blood transfusion were taken into consideration. The bypass time in acyanotic cases ranged between 22 and 45 minutes (average 36 minutes), whereas in cyanotic patients, due to more intricate nature of the operation, the bypass time ranged between 49 and 87 minutes (average 61 minutes). The average blood loss in 24 hours (postoperative) as assessed by thoracotomy drainage in Group I cases (Table 1) was 7ml./kg. (range 5-13ml./kg.) and in Group II cases (Table 2) it was 10.8ml./kg. (range 6-19ml./kg.) and the total blood transfusion received by Group I cases and Group II cases were 38ml./kg. (range 26-60ml./kg.) and 47ml./kg. (range 20-74ml./kg.) respectively.

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TABLE 1—SHOWING THE PARTICULARS OF THE PATIENTS OF GROUP I, VOLUME OF TRANSFUSION, VOLUME OF BLOOD LOSS AND DURATION OF BYPASS DURING CARDIO-PULMONARY BYPASS SURGERY

No.	Name Age (years) Sex	Body weight (kg)	Diagnosis	Blood		Duration of pump (minutes)	Complication
				Transfusion ml./kg.	Loss ml./kg.		
1	K.B. 10 M	30	ASD	40	8	45	—
2	S.A. 28 M	40	ASD	30	5	38	Cerebral air embolism
3	M.N. 22 M	42	PS,ASD*	30	5	40	—
4	K.K.S. 16 M	34	ASD	37	6	36	—
5	K.D. 8 F	28	ASD	60	10	23	Pump restarted
6	P.B. 15 F	33	ASD	26	6	39	—
7	A.K. 11 F	29	ASD	40	7	33	—
8	K.S. 16 F	28	PS**	40	6	22	—
9	R.C.D. 14 M	28	ASD	30	6	39	—
10	D.C. 29 F	36	ASD	26	6	36	—
11	J.D. 6 M	20	VSD	60	13	45	—

PS—Pulmonary stenosis; ASD—Atrial septal defect
VSD—Ventricular septal defect
*Anomalous pulmonary venous drainage
**Valvular and infundibular stenosis

The fall of haemoglobin or haematocrit level (Table 3) could not be accounted for by blood loss alone and this could be due to haemodilution which was to the extent of 10-30 per cent because of priming fluid and additional transfusion during surgical procedure. Although rise of plasma haemoglobin was evident in both the groups, plasma was cleared of free haemoglobin within 24 hours and the rise of serum bilirubin was negligible.

Thrombocytopenia was a marked feature in cases of both Group I and Group II. Prothrombin time and thromboplastin time (KCCT) were prolonged in both the groups but more so in cyanotic cases immediately after bypass (Table 4). The post-bypass samples of blood also showed marked fibrinogenopenia and fibrinolytic activity as evidenced by shortening of euglobulin clot lysis time. Fibrin monomer could be detected qualitatively in 6 out of 11 cases of Group I and in all the 7 cases of Group II. Therefore, the patients undergoing bypass surgery in the present series presented mild degree of haemolysis of red cells, thrombocytopenia, fibrinogenopenia, prolongation of prothrombin time, increased fibrinolytic activity and fibrin monomer in postoperative samples of blood but the overall effect was more pronounced in cyanotic heart diseases (Table 4).

For clinical correlation of laboratory findings of the haemostatic defects, the patients were termed as bleeders when the thoracotomy drainage exceeded 10 ml./kg./24 hours, i.e., an arbitrary border line between normal and abnormal postoperative oozing. In Group I cases, only one subject (J.D.) exceeded the limit and another one (K.D.) was on the border line (Table 1). The recovery of the patients of Group I was uneventful except in one case (S.A.) who developed features of cerebral air embolism. In Group II cases on the other hand 5 out of 7 cases were potentially bleeders as per above criteria as the thoracotomy drainage exceeded the limit of normal postoperative oozing (Table 2). However, there was only one mortality (J.P.) due to excessive postoperative bleeding, but in this case also oozing stopped temporarily with drip infusion of antifibrinolytic agent (Schedule C). The patient succumbed because timely transfusion of fresh blood could not be arranged. Another patient (B.M.S.) of the same group also died on the 8th postoperative day, without having any obvious bleeding manifestations. He had developed haemorrhagic infarction of the middle lobe of the only functioning lung. The laboratory data of coagulation study, therefore, presented a much more serious picture of coagulation defects than the manifest clinical bleeding or fatal bleeding episode.

TABLE 2—SHOWING PARTICULARS OF THE PATIENTS OF GROUP II, VOLUME OF TRANSFUSION, VOLUME OF BLOOD LOSS AND DURATION OF BYPASS DURING CARDIO-PULMONARY BYPASS SURGERY

No.	Name Age (years) Sex	Body weight (kg.)	Diagnosis	Blood		Duration of pump (minutes)	Complication
				Transfusion ml./kg.	Loss ml./kg.		
1	S.A. 8 M	22	Fallot's tetralogy	74	12	55	Nil
2	I.M. 7 M	18	Fallot's tetralogy	60	10	49	Nil
3	B.M.S. 13 M	29	Fallot's tetralogy with unilateral pulmonary stenosis	50	10	87	Death due to haemorrhagic infarct of lung
4	J.P. 20 M	48	Double outlet right ventricle with pulmonary, infundibular and valvular stenosis and ASD	40	19	55	Excessive bleeding; died on 3rd postoperative day
5	S.B. 10 M	20	Double outlet right ventricle with pulmonary, infundibular and valvular stenosis	60	10	77	Nil
6	H.H. 16 M	44	ASD and PS	26	8.5	58	Nil
7	M.P.K. 17 M	46	ASD and PS	20	6	50	Nil

TABLE 3—SHOWING VALUES OF BLOOD HAEMOGLOBIN, PACKED CELL VOLUME (PCV), PLASMA HAEMOGLOBIN AND SERUM BILIRUBIN LEVELS IN PRE- AND POST-BYPASS SAMPLES

	Group I		Group II	
	Pre-	Post-	Pre-	Post-
Blood haemoglobin g.%	10.4 (8.8-15.8)	8.8 (6.7-14)	16.6 (13-18)	13.6 (11.8-15)
Packed cell volume %	34 (27-48)	28 (18-42)	50 (40-57)	40 (34-48)
Plasma haemoglobin mg.%	3.6 (1.6-6.6)	5.4 (3.8-18)	2.6 (1.8-5)	12 (6-19)
Serum bilirubin mg.%	0.8 (0.2-1)	1.4 (0.8-2.4)	0.6 (0.2-0.8)	2.4 (0.8-2.8)

Transfusion of fresh blood (Schedule D) corrected in most of the cases any abnormal postoperative oozing. Antifibrinolytic drug was administered at some stages during or after bypass surgery in Group II cases and it was administered whenever clinical oozing seemed to be more than normal in spite of normal clotting time after neutralisation of heparin, without waiting for detailed coagulation tests. The value and advisability of the procedure have been discussed in relation to inherent haemostatic defects in cyanotic heart diseases.

TABLE 4—SHOWING THE HAEMOSTATIC PROFILE OF CYANOTIC AND ACYANOTIC GROUPS OF CASES DURING EXTRACORPOREAL CIRCULATION

	Group I		Group II	
	Pre-	Post-	Pre-	Post-
Platelet × 10^3 /cmm.	290 (320-200)	88 (109-74)	188 (200-160)	56 (68-30)
Prothrombin index (%)	98 (105-94)	58 (66-48)	100 (105-98)	40 (44-30)
KCCT in seconds	48 (38-55)	68 (50-78)	50 (40-58)	84 (74-100)
Fibrinogen (mg.%)	320 (288-352)	140 (116-170)	200 (180-240)	80 (60-110)
Euglobulin clot lysis time in minutes	180 (150-250)	150 (120-210)	200 (180-240)	60 (20-80)
SDPS test	Neg.	Positive (6 cases)	Neg.	Positive (7 cases)

KCCT—Kaolin cephalin clotting time
SDPS—Serial dilution protamine sulphate

DISCUSSION

Haemostatic mechanism of the body was undoubtedly deranged during cardio-pulmonary bypass surgery but the degree of haemostatic defects as measured by coagulation studies in the laboratory did not always correspond to the actual clinical or haemorrhagic complications. Therefore it was thought all the more imperative to find out a parameter to assess the degree of postoperative bleeding so that effective therapeutic measures could be instituted at the appropriate time. In this paper thoracotomy drainage of 10ml./kg./24 hours was taken arbitrarily as the upper limit of normal postoperative oozing. In acyanotic subjects (Group I) thoracotomy drainage was within that range except in one patient, whereas in cyanotic subjects this limit was exceeded in most of the cases but fatal haemorrhagic episode was observed only in one subject. The laboratory data on the other hand gave a much more serious picture of coagulation defect than the manifest bleeding state during postoperative period. This view is also shared by de Gabriele (1963) who observed that laboratory evidences of coagulation defect were not always associated with haemorrhagic complications. Transfusion of large volumes of blood as required during bypass surgery could alter the haemostatic profile (Stefanini, 1962) and the plasma clotting factors in cyanotic heart diseases, already reduced to a critical level due to polycythaemia, could be further depleted due to haemodilution during priming (Singh *et al.*, 1961).

Fibrinogenopenia, depletion of plasma labile factors and gross degree of thrombocytopenia as were observed during bypass surgery point towards the clinical state of defibrination. Mild degree of haemolysis was constantly observed during bypass surgery in the cyanotic subjects and release of red cell or platelet phospholipid might as well have caused generation of active thromboplastin (Quick, 1960). The mechanism of red cell haemolysis during or after extracorporeal circulation is a subject of considerable interest (Wallace and Blakemore, 1970). Even after adequate heparinisation as per Schedule A some degree of generation of thrombin did take place as was evident by the presence of fibrin monomer. This observation has an important bearing on the post-bypass neutralisation of heparin by commercial protamine sulphate whose strength may vary from batch to batch, and an excess of protamine sulphate in the system can further enhance the intravascular coagulation if administered without proper titration. It was thought unwise to neutralise all traces of heparin in post-bypass phase as excess of heparin is known to prevent microclot formation in the vascular bed. For monitoring heparin in the system, whole blood clotting time was preferred to thrombin clotting time which tends to overestimate the requirement of protamine sulphate in the platelet-poor plasma (Hardisty and Ingram, *loc. cit.*)

Other probable causes of postoperative bleeding during extracorporeal circulation are activation of fibrinolytic enzymes by thrombin generated due to prolonged contact of blood with foreign surface and gross degree of thrombocytopenia (Sharp and Eggleton, 1963; Salzman, 1963; Jenevein and Weiss, 1964). Excess of fibrin monomer, as was observed in all the cases of Group II, is known to form friable clot with plasma fibrinogen and the haemorrhagic tendency becomes further aggravated due to hepatic dysfunction often associated with prolonged anaesthesia (Fletcher and Alkjaersig, 1973). Although fibrinolytic activity appeared greatly enhanced in the cyanotic patients, the appropriate dose and time of administration of antifibrinolytic agent were assessed by the clinical bleeding state. The theoretical limitation of routine use of antifibrinolytic agent was also considered as the clearance rate of fibrin monomer is impeded due to blocking effect of antifibrinolytic agents on the reticuloendothelial system (Lee, 1962). This view has been substantiated by experimental works where after infusion of thrombin or thromboplastin massive deposits of fibrin and necrotic infarcts in kidneys were observed in animals when treated with antifibrinolytic agents, whereas in untreated animals such features were not present (Margaretten *et al.*, 1964).

Thrombocytopenia was a constant finding but there was no purpura or mucous membrane bleeding, and this shows that the Schedule A dose of heparin as such had no untoward effect on the capillary endothelium.

In conclusion we would like to emphasise that routine use of antifibrinolytic agents should not be undertaken even in cases of cyanotic heart diseases undergoing bypass surgery without prior assessment of haemostatic profile of the patients. Fresh blood transfusion and traces of heparin in the circulation would afford a better protection against increasing haemostatic derangement as the excessive postoperative oozing appears primarily due to intravascular coagulation following extracorporeal circulation. However, we have not yet evaluated such factors as blood viscosity, degree of oxygen unsaturation or the effect of polycythaemia on haemostasis during bypass surgery; these are separate matters for further study.

SUMMARY

Haemostatic profile in cases of cyanotic congenital heart diseases during and after cardio-pulmonary bypass surgery has been investigated and compared with acyanotic cases undergoing similar operation. The method of collection of blood, heparinisation schedule, post-bypass neutralisation of heparin, degree of red cell haemolysis, thrombocytopenia and utilisation of clotting factors have been evaluated. In cyanotic heart

diseases undergoing bypass surgery even after adequate heparinisation of blood as per schedule there were evidences of consumption of factors of coagulation and activation of thrombin. The degree of clotting factor defects as measured in the laboratory did not always correspond to the manifest clinical bleeding nor did it indicate haemorrhagic complication in post-bypass period. In the presence of intravascular coagulation the limitation of protamine sulphate or antifibrinolytic agent has been considered to formulate a therapeutic schedule for post-bypass management of such cases.

ACKNOWLEDGMENT

The authors are grateful to the Principal-Superintendent, Nilratan Sircar Medical College and Hospital, for facilities and to Prof. B. P. Chatterjea, M.S., F.R.C.S., Director-Professor of Surgery (Retd.), for his cooperation at every stage of the work.

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3

Risk Factors of Digoxin Intoxication

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[Received for publication February 22, 1974]

Serum digoxin concentration is an important determinant in the uptake of digoxin by the myocardium (Doherty, 1968; Roberge *et al.*, 1970). However, in human disease states it is not the only factor in the development of digitalis toxicity (Butler, 1972). Relatively high serum digoxin concentrations have been observed in a significant number of non-toxic patients, whereas few digitalis intoxicated patients have levels more commonly encountered in non-toxic subjects (Smith and Haber, 1970; Beller *et al.*, 1971). These discrepancies between serum digoxin concentration and the presence or absence of toxicity denote an individual difference in myocardial digoxin uptake and in the sensitivity of the myocardium to the effects of the drug (Doherty *et al.*, 1967; Lukas, 1971).

It is known that electrolyte disturbances, autonomic influences, metabolic alterations, drugs and hormones may influence the uptake of digoxin by the myocardium. On the other hand, certain other factors may render the myocardium more sensitive to a given tissue digoxin concentration, without enhancing its uptake (Butler, *loc cit.*). Such factors which increase the risk of digoxin toxicity by increasing either the sensitivity or the uptake of digoxin by the myocardium may be regarded as risk factors of digoxin intoxication.

There is uncertainty about the role of risk factors in the development of digoxin intoxication. This study, therefore, was designed with 2 aims—to find out the serum digoxin levels in toxic patients associated with risk factors; and to highlight their importance, if any, in the manifestations of digoxin toxicity.

MATERIAL AND METHOD

This prospective study was conducted in the medical wards of S. S. Hospital, B.H.U., Varanasi,

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from January, 1972 to April, 1973. The criteria for the presence or absence of toxicity were based upon those accepted by Smith and Haber (*loc. cit.*) and Beller *et al.* (*loc. cit.*).

Clinical, radiological, electrocardiographic and other necessary investigations were done in all the patients to find out the cause and nature of heart failure. Other biochemical data like blood urea, serum creatinine, potassium, calcium, sodium, chloride and magnesium were estimated by standard methods.

Serum digoxin assay—Serum digoxin estimation was done by radioimmunoassay (Smith *et al.*, 1969).* The specificity and sensitivity of this method is excellent and it can detect levels of digoxin well below 0.2 µg./ml. (Butler, *loc. cit.*). The counting was done in a liquid scintillation counter.

Blood samples—The blood samples in the toxic group were collected 8 to 24 hours after administration of the last dose of digoxin at the time of electrocardiographic evidence of digoxin toxicity. However, in the non-toxic group the samples were collected 7 hours after administration of the last dose of digoxin.

RESULTS

Clinical data—Fifty-two toxic patients (mean age—33.2±15.8 years; mean body weight—49.0±9.9 kg.) were given 0.62±0.20 mg. of digoxin per day and 46 non-toxic patients (mean age—27.3±14.8 years; mean body weight—46.0±10.4 kg.) required 0.54±0.18 mg./day of digoxin for the control of heart failure. There were no significant differences in the incidence of male sex and class III and IV heart failure in between the 2 groups. However, non-cardiac manifestations of digoxin toxicity were very much prevalent in the toxic group as compared to the non-toxic group.

Biochemical data—There was no significant difference in the mean serum creatinine, sodium, potassium, chloride, calcium and magnesium concentrations of the 2 groups. However, mean blood urea in the non-toxic group was 32.2±20.5 mg./100 ml., and in the toxic group it was 45.6±32.1 mg./100 ml. The differences were statistically significant ($P<0.01$).

Risk factors—Analysis of risk factors revealed that the incidence of acute cardiac damage (28.8 per cent), advanced age (25.0 per cent), hypomagnesaemia (50.0 per cent) and uraemia (23.0 per cent) was higher in the toxic group as compared to the non-toxic group (Table 1). Furthermore, in some of the patients multiplicity of risk factors was noted which was more prevalent in the toxic group as is obvious from Table 2. Patients with acute myocardial damage included acute myocardial infarction, acute myocarditis, subacute bacterial endocarditis and acute rheumatic carditis.

Serum digoxin levels—Mean serum digoxin levels in 46 non-toxic and 52 toxic patients were 2.27±0.83 µg./ml. and 3.74±1.34 µg./ml. respectively. However, the differences were highly significant ($P<0.001$). It was further observed that when 10 cases of atrial fibrillation were excluded from the non-toxic group the mean serum digoxin level became 2.00±0.71 µg./ml. (Fig. 1).

TABLE 1—SHOWING THE INCIDENCE OF RISK FACTORS

Risk factors	Non-toxic (46 cases)	Toxic (52 cases)
Acute cardiac damage	7 (15.2%)	15 (28.8%)
Cor pulmonale	7 (15.2%)	6 (11.5%)
Severe anaemia and cachexia	5 (10.9%)	3 (5.7%)
Pulmonary embolism	—	1 (1.9%)
Old age (more than 50 years)	5 (10.9%)	13 (25.0%)
Hypomagnesaemia - (less than 1.5 mEq./l.)	17 (36.9%)	26 (50.0%)
High blood urea (more than 50 mg./100ml.)	5 (10.9%)	12 (23.0%)
Cerebrovascular accidents	—	2 (3.8%)
Cortisone therapy	—	2 (3.8%)

TABLE 2—SHOWING RELATIONSHIP OF SERUM DIGOXIN IN TOXIC PATIENTS WITH AND WITHOUT RISK FACTORS

		Toxic with risk factors			
	Toxic without risk factors	Acute cardiac damage	Hypomagnesaemia	Old age	Other risk factors
No.	27	15	26	13	10
Mean µg./ml.	4.2	3.44	3.23	3.17	2.76
S.D.	1.56	2.06	0.68	1.05	0.70
Range	1.8--10.1	1.3--10.2	1.8--5.3	1.2--4.7	0.9--3.5
"t"	—	1.18	3.03	2.51	3.891
"p"	—	NS	<0.001	<0.02	<0.001

NS—Nonsignificant

Tables 3, 4 reveal that the patients without risk factors developed digoxin toxicity at higher levels of serum digoxin (4.20±1.56 µg./ml.) in comparison to patients having risk factors (Fig. 1).

DISCUSSION

It has been repeatedly emphasised that the dosage of digitalis varies from patient to patient

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*The chemicals for the assay of serum digoxin were imported from Wien Laboratory, Succasunna, U.S.A.

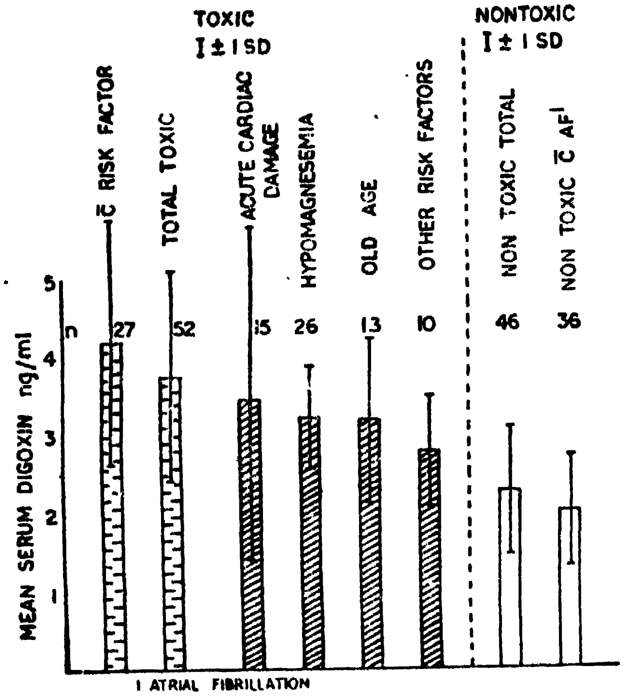

FIG. 1—Showing Mean Serum Digoxin Level in Relation to Various Factors

TABLE 3—Showing Effect of Conglomeration of various Risk Factors on Digoxin Toxicity in Non-Toxic Patients

Risk factors	Sl. No.	Old age	Hypo-magnesaemia	CVA	High blood urea
Acute cardiac damage	1	—	—	—	—
	2	—	+	—	—
	3	+	—	—	—
	4	+	—	—	—
	5	—	—	—	—
	6	—	—	—	—
	7	—	+	—	—
Cor pulmonale	1	+	—	—	+
	2	—	—	—	—
	3	—	—	—	—
	4	—	—	—	—
	5	—	+	—	—
	6	—	—	—	—
	7	—	+	—	—
Severe anaemia and cachexia	1	—	—	—	+
	2	—	—	—	—
	3	+	—	—	—
	4	—	—	—	—
	5	+	—	—	—

CVA—Cerebrovascular accidents

TABLE 4—Showing Effect of Conglomeration of various Risk Factors on Digoxin Toxicity in Toxic Patients

Risk factors	Sl. No.	Old age	Hypo-magnesaemia	CVA	Corti-sone thera-py	High blood urea
Acute cardiac damage	1	+	+	—	—	—
	2	—	—	—	—	+
	3	—	+	—	+	+
	4	—	—	—	—	—
	5	—	—	+	—	—
	6	—	—	—	+	+
	7	—	+	—	—	—
	8	—	+	—	—	—
	9	—	—	—	—	+
	10	+	+	—	—	—
	11	—	+	+	—	—
	12	—	—	—	—	—
	13	—	—	—	—	—
	14	+	—	—	—	+
	15	—	—	—	—	—
Cor pulmonale	1	+	+	—	—	—
	2	—	+	—	—	+
	3	—	+	—	—	—
	4	+	+	—	—	—
	5	+	+	—	—	—
	6	—	+	—	—	—
	7°	—	+	—	—	+
Severe anaemia and cachexia	1	—	+	—	—	—
	2	+	+	—	—	—
	3	—	—	—	—	—

°Pulmonary embolism

and also it may vary from time to time in the same patient (Chung, 1969). It is also apparent that toxic and non-toxic digoxin concentrations may also be different from patient to patient (Butler, *loc. cit.*). However, it appears that more than 50 per cent of toxic manifestations do occur as a result of relative over-dosage (Koch-Weser, 1972), that is, they result from dosages that are too high for the patients affected, as for example, in patients with abnormal renal functions.

It is apparent from Tables 3, 4 that conglomeration and prevalence of risk factors were higher in the toxic patients. Increased sensitivity to digoxin in patients with old age (Dall, 1965), class III and IV heart failure (Von Capeller *et al.*, 1959; Beller *et al.*, *loc. cit.*), cor pulmonale (Hargreave, 1965; Beller *et al.*, *loc. cit.*), acute myocardial infarction (Shrager, 1957; Morris *et al.*, 1969), subacute bacterial endocarditis and acute rheumatic carditis, thyroid state and severe anaemia with cachexia (Friedberg, 1966), cerebrovascular accidents (Rodensky and Wasserman, 1961), congenital and cyanotic heart disease and effects of surgery (Mukerjee, 1972), renal insufficiency (Dubnow and Burchell, 1965; Doherty, *loc. cit.*), hypokalaemia (Lown and Levine, 1954; Dubnow and Burchell, *loc. cit.; Prindle et al.*, 1971), hypomagnesaemia (Beller *et al., loc. cit.;* Seller, 1971) and intake of drugs (Tanabe, 1968) has been observed by many investigators.

Recently Beller *et al.* (*loc. cit.*) observed higher prevalence of atrial fibrillation in a group of toxic patients possibly as a result of advanced heart disease. These patients required higher digoxin concentrations to control the ventricular rate as observed in this study (Chamberlain *et al.*, 1970; Redfors, 1972). However, in a recent study, Johnston *et al.* (1972) reported that age, severity or type of cardiac disease and plasma potassium levels in the patients bore no relationship to the development of toxicity, but a majority of toxic patients had renal insufficiency.

It is apparent from Table 2 that in patients associated with hypomagnesaemia, old age and other risk factors, the mean serum digoxin levels were 3.23±0.68 μg./ml., 3.17±1.05 μg./ml. and 2.76±0.70 μg./ml. respectively, whereas in patients without risk factors the mean digoxin level was 4.2±1.56 μg./ml. However, the differences were statistically significant. Patients associated with acute cardiac damage had low digoxin levels as compared to patients without risk factors, but the differences were insignificant. Digoxin intoxication at lower levels of digoxin has also been observed by Smith and Haber (*loc. cit.*) and Beller *et al.* (*loc. cit.*) in patients associated with acute myocardial infarction, old age, hypertension and arteriosclerosis, heart disease and chronic lung disease.

This shows that hypomagnesaemic patients (<1.5 mEq./l.) are more sensitive to the effects of the drug. On the other hand, patients with old age develop increased risk to digoxin toxicity as a result of higher incidence of arteriosclerotic and ischaemic heart disease and age related myocardial alterations (Beller *et al., loc. cit.;* Butler, *loc. cit.*).

Cor pulmonale, pulmonary embolism and severe anaemia are known to cause hypoxia and myocardial damage. In acute myocardial damage, increased automaticity, irritability and ischaemia may predispose to cardiac arrhythmias.

Patients with impaired renal function are susceptible to the development of digoxin toxicity while receiving digoxin in doses that are well tolerated by patients with normal renal function as the drug is not excreted. Renal insufficiency as a risk factor of toxicity has been observed by many investigators (Smith and Haber, *loc. cit.;* Beller *et al., loc. cit.;* Johnston *et al., loc. cit.*).

It should be emphasised that the presence of a risk factor predisposes the patient to the risk of digoxin toxicity at comparatively lower serum levels of digoxin. Conglomeration of risk factors in a patient further increases the risk of toxicity. These observations of the present study confirm the previously held views of other observers when new techniques for serum digoxin assay did not exist. Estimations of serum digoxin levels in patients associated with risk factors will be of great value to the physician in determining the dosage of the drug to be administered to such patients. Naturally, these patients need digitalisation with low dosage schedule and low maintenance doses, and frequent assay of the drug in the blood should be carried out to prevent toxicity and consequent mortality.

SUMMARY

A prospective hospital study of 98 patients in which 52 were toxic, revealed that 25 of these toxic patients had one or more risk factors. Acute cardiac damage (28.8 per cent), advanced age (25.0 per cent), hypomagnesaemia (50.0 per cent) and other risk factors were very much prevalent and the corresponding serum digoxin levels were significantly lowered as compared to patients without risk factors. Some patients had multiple risk factors. We conclude that digoxin toxicity in patients associated with risk factors manifests at significantly lower digoxin concentrations. Thus, presence of such factors increases the risk of toxicity and, therefore, digitalisation with lower dosage schedule, administration of lower maintenance doses, and more frequent estimation of digoxin and dosage regulation accordingly, will be of great help in the prevention of toxicity and mortality due to this drug.

ACKNOWLEDGMENT

Our thanks are due to Padmashree Prof. K. N. Udupa, Director, Institute of Medical Sciences, B.H.U., for his kind permission to publish this paper. Our thanks are also due to Mr. Angenaloo of the Department of Biochemistry for doing the counting in liquid scintillation counter. Lanoxin brand of digoxin used in the present study, was kindly donated by Messrs. Burroughs Wellcome Co. Ltd.

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PRACTITIONERS' SERIES

Rhinosporidiosis†

C. S. ANAND*, S. K. GUPTA**
(MRS.) S. SRIWASTAVA***

Rhinosporidiosis is a chronic infestation of mucous membrane of the nose, eyes, larynx, ears and occasionally genital organs, and is characterised by formation of friable, strawberry like, sessile or pedunculated polypi. Although it is caused by *Rhinosporidium seeberi*, the organism has not yet fulfilled Koch's postulations; and it has been neither cultured nor transmitted to man or animal by experimental inoculations. Malbram in 1892 reported the first case of rhinosporidiosis from Argentina. Subsequently it was recognised that the infection was prevalent in North and South America, South Africa, parts of Asia and Europe. It is endemic in India and Ceylon. Allen and Dave (1936) reported 60 cases in India in a period of 18 months, and Karunaratne (1964) collected 104 cases in Ceylon. Satyanarayana (1960) reported rhinosporidiosis in a record number of 255 cases. The frequent occurrence of this condition has given us an opportunity to study the disease in detail and enabled us to discuss certain points connected with its nomenclature, prevalence and management.

MATERIAL

Approximately 15,000 patients, who attended the E.N.T. Department (out-patient department) between August, 1971 and July, 1972 were screened for rhinosporidiosis and 11 cases of this disease were discovered and investigated. In each case, a detailed history of personal hygiene, bathing in stagnant water tanks, obstruction in nose, bleeding from the nose, change in voice was taken. Detailed examination of nasal and oral cavities was performed to determine the size, shape and anatomical attachment of the polyp. Subsequently the polyp was excised and subjected to detailed histopathological examination. A resume of 11 cases showing age, sex, symptoms, site and treatment is given in Table 1.

OBSERVATIONS

Clinical features—The symptomatology of rhinosporidiosis varies according to the site and size of the lesion. The most common complaint of our patients was epistaxis (9 cases). It was followed by nasal obstruction (7 cases) and itching sensation in nose (3 cases). Mucopurulent discharge was noticed in 1 of the cases. One case reported change of voice and difficulty in deglutition. In almost all cases, the growth arose from nasal cavity and in 2 of them it hanged down over the upper lip.

In Case 9, there was extension of the growth towards the nasopharynx and it hanged down below the soft palate as a papillomatous mass. In all the cases the lesion was unilateral, except in one, in whom it was bilateral.

Histopathology—The sections showed typical histopathological changes as seen in rhinosporidiosis. The epithelial lining was normal (tall columnar) but showed squamous metaplasia at places. The continuity of the epithelial lining was broken at places (Fig. 1).

Subepithelial tissue showed inflammatory granulation tissue formation and infiltration of chronic inflammatory cells, plasma cells as well as eosinophils. At places there was huge collection of chronic inflammatory cells. A few areas

---

†Paper read at the Silver Jubilee Conference of the Association of Otolaryngologists of India, Bombay

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TABLE 1—SHOWING CLINICAL FEATURES AND TREATMENT OF 11 CASES

Case No.	Age (years)	Sex	Symptoms with duration (in months)		Site of lesion	Aetiological factors	Treatment	Past history
1.	25	F	Epistaxis Itching in nose	1 1	Left nasal fossa	Herds of cattle in house	Excision with cauterisation of base	—
2.	25	F	Epistaxis Nasal obstruction	18 18	Both nasal fossa from roof	—	—do—	A similar mass was excised 4 years ago
3.	14	M	Itching in nose Rhinorrhoea	4 4	Left nasal fossa	Swimming in ponds where cattle also take bath	—do—	—
4.	11	M	Nasal obstruction	3	—do—	—	—do—	—
5.	23	M	Epistaxis Nasal obstruction	4 4	—do—	—	—do—	Two months ago a similar mass was excised
6.	16	M	Epistaxis Nasal obstruction	6 6	—do—	—	—do—	—
7.	22	M	—do—		—do—	—	—do—	—
8.	15	M	Epistaxis Itching in nose	2 2	—do—	—	—do—	—
9.	30	M	Epistaxis Change of voice Nasal obstruction	1 4 12	Left nasal fossa, naso-oropharynx	—	Excision and delivered through oral cavity	Seven years ago had a mass in left nasal fossa which was excised
10.	17	F	Epistaxis	5	Left inferior turbinate	Swimming in ponds during childhood	Excision and cauterisation	—
11.	16	F	Epistaxis Nasal obstruction	2½ 2½	Left nasal fossa	—	—do—	—

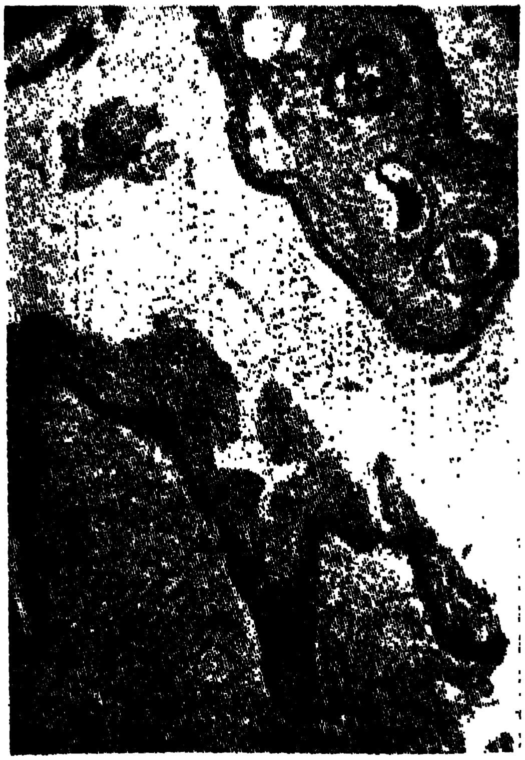

FIG. 1—SHOWING PHOTOMICROGRAPH WITH NORMAL EPITHELIAL LINING BUT SQUAMOUS METAPLASIA AT PLACES

showed foreign body type of giant cells. Haemorrhagic areas were seen at places.

Fungus—Rhinosporidia were seen in various stages of its development, i.e., immature cysts immediately beneath the epithelium, mature cysts with typically double layered chitinous walls and innumerable spores inside, deeper in the subepithelial tissue. The mature cysts bursting and liberating the mature spores at the surface epithelium were also seen (Fig. 2).

In the area of granulation tissue formation one could see laying down of collagen tissue, proliferation of fibroblasts, many newly formed capillaries and few inflammatory cells.

DISCUSSION

Nomenclature—The term 'rhinosporidiosis' is widely used and has been incorporated in the text-books. It is synonymous with a chronic infection of mucous membrane caused by *Rhinosporidium seeberi* or *Rhinosporidium kinealyi*. Anatomically, 'rhino' represents the nasal cavity; therefore, at times it seems that this particular fungus involves the nasal cavity only. Undoubtedly the nose is the most common site of infection, but it is well known that the fungus is capable of attacking eye, lacrimal sac, ear, skin, vagina and

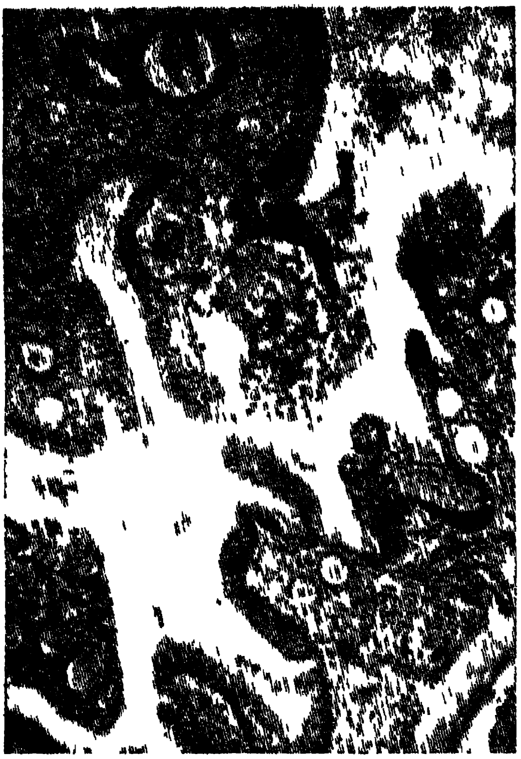

Fig 2—Showing Photomicrograph with Mature Cysts Bursting and Liberating Mature Spores

scrotum also. This generalised manifestation of the organism raises serious objections regarding the continuation of the term 'rhinosporidiosis'. In our opinion, this term should be given up and replaced by 'sporidiosis', which may further be affixed or suffixed depending upon the site of involvement (such as, otosporidiosis, oculosporidiosis, etc.).

Prevalence—It is recognised that rhinosporidiosis is endemic in India, but the exact prevalence rate of the disease is not yet established. The available reports suggest that there exists a regional variation in the prevalence of rhinosporidiosis. Moreover, it is difficult to determine the correct prevalence rate unless it is especially looked for in routine clinical and subsequent histopathological examinations. In our present analysis, the prevalence rate comes to 0.074 per cent of all types of E.N.T. patients. Corresponding figures from other parts of the country are lacking. A review of the literature indicates that the disease is relatively more prevalent in Orissa, Andhra, Tamilnadu, Mysore, Kerala and parts of Madhya Pradesh. In the Raipur region of M.P., rhinosporidiosis shows a greater tendency for extranasal involvement (eye, skin and sole). In some parts of South India, bovine form of the disease is quite striking.

The disease may develop at any age, commonly between 5 and 55 years, but is more common in adolescents, as is evident from the present study. All our cases belonged to the age group of 11 to 30 years. Males were more often affected than females. Karunaratne (1939) reported 87.8 per cent incidence in males. In our series, it comes to 63.6 per cent.

There is a general belief that the disease is transmitted through certain occupations. Mandlick (1937) suggested a higher incidence of the infection in the sand divers of India who habitually dive and swim in stagnant water. Jain (1967) considers that bathing in dirty tanks at the time of religious festivals significantly contributes to the transmission of infection in the religious community. However, there is no substantial evidence put forward proving this speculation. It has also been suggested that widespread and indiscriminate use of antibiotics and corticosteriods enhances the prevalence of rhinosporidiosis. Nevertheless, the authenticity of such a statement remains in doubt in the absence of any proven clinical or laboratory evidence. If these drugs can render a laboratory animal susceptible to this obstinate fungus, it would be a great breakthrough in the establishment of Koch's postulations for this organism also.

Rhinosporidiosis is often considered as a benign lesion and is seldom fatal. It is notorious for its chronicity and tendency to recurrence after surgical extirpation. Paradoxically, it has been reported that small lesions might disappear spontaneously after 8-9 years (Allen and Dave, *loc. cit.*). While dealing with cases of rhinosporidiosis, one must not consider it a superficial mucosal lesion, because it may cause systemic dissemination with fatal outcome (Rajam *et al.*, 1955). Karunaratne (1964) also argued to put rhinosporidiosis in the group of deep mycosis. It is, therefore, logical to tackle the superficial lesions carefully and completely. At times, cauterisation of the operaed site assures double security against possible recurrence.

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CASE NOTES

1

Primary Abdominal Pregnancy Complicated by Intestinal Obstruction

SUBRATA KUMAR CHATTERJEE*
SAKTIPRASAD CHATTERJEE**
PIKU CHAUDHURI***

Abdominal pregnancy means gestation free in the peritoneal cavity rather than between the leaves of the broad ligament or in a greatly dilated fallopian tube. A case of primary abdominal pregnancy complicated by intestinal obstruction is presented because of its rarity.

CASE REPORT

Mrs S., aged 30 years, was admitted to the Chittaranjan Hospital, Calcutta National Medical College, on 20-5-1974 with a history of pain in the abdomen for 1½ months preceded by a period of 14 weeks amenorrhoea followed by vaginal bleeding, severe vomiting and constipation for last 2 weeks. She was married for last 18 years with 3 previous pregnancies and uneventful normal deliveries, all children alive and well. The last childbirth was 3 years ago. The previous menstrual history was of regular cycle with normal flow, last normal menstrual period being on 29.12.1973. There was no history of any medical disorder or abdominal surgery in the past.

The patient looked very pale, ill and anaemic with signs of dehydration. The abdomen was distended with features of intestinal obstruction. There was an irregular firm tender swelling arising from pelvis and occupying the whole lower abdomen, extending about 4 inches above the level of the symphysis pubis. The vagina looked pale, the lump was occupying the whole pelvis, and was very tender the uterus could not be felt separately. The cervix was drawn up and pushed anteriorly, flush with the vagina, it looked healthy, the os admitting the tip of the index finger. No product of conception was felt. The examining finger was slightly stained with blood.

A provisional diagnosis of ruptured ectopic pregnancy with pelvic haematocele complicated by intestinal obstruction was made and laparotomy was performed on the same day after resuscitating the patient by gastric suction, blood transfusion and I.V. fluid infusion.

The abdomen was opened by a right infra-umbilical paramedian incision. An irregular lump was seen covered by blood clots partly occupying the pouch of Douglas and partly the lower abdomen. It was surrounded by intestine and omentum, densely adherent to it. The lump was about 6 inches × 4 inches in size and oval in shape. The large intestines were grossly distended and partly adherent to the lump with multiple adhesive bands. The uterus was found anteriorly, normal in size, free from adhesions with the lump. There was no evidence of any recent or remote perforation or any other abnormality in it. The right fallopian tube and ovary looked normal and were free fom adhesion. The left fallopian tube and ovary were slightly adherent to the lump but looked otherwise normal without any evidence of perforation or rupture. Abdominal ostia of both the fallopian tubes looked normal and no bleeding was seen through the ostia neither there was any haematoma. The lump contained a dead foetus of about 14 weeks size surrounded by layers of blood clot (Fig 1) most of the sac wall and placenta were dissected out from the surrounding structures and removed leaving behind a part of the sac wall and placenta deeply adherent to the large intestines and omentum. The intestinal adhesive bands were divided and the intestines were freed from adhesions as far as possible. Both the fallopian tubes were removed totally as a procedure of sterilization along with the left ovary and were sent for histological examination for evidences of pregnancy within these structures.

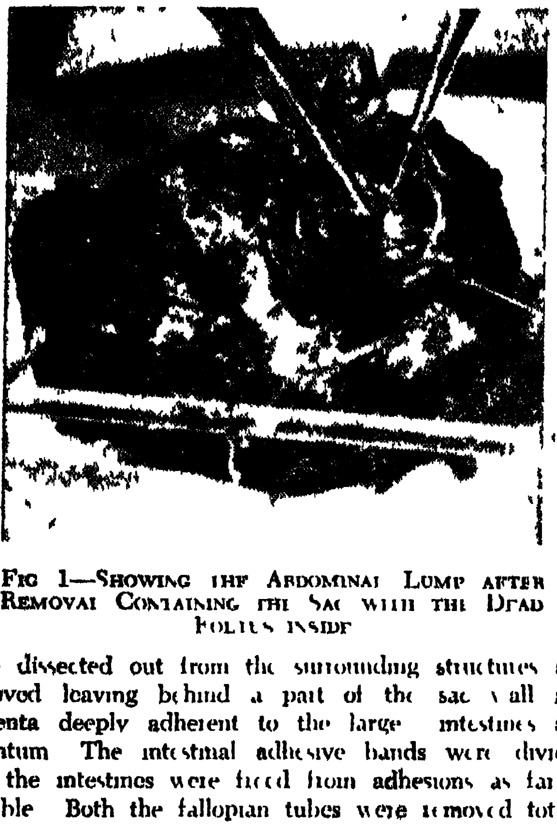

FIG 1—SHOWING THE ABDOMINAL LUMP AFTER REMOVAL CONTAINING THE SAC WITH THE DEAD FOETUS INSIDE

Postoperatively features of intestinal obstruction continued for a few days and the patient was treated by I.V. fluid, gastric suction, blood transfusion and antibiotics.

On the 10th postoperative day the patient developed pulmonary embolism leading to congestive cardiac failure and was treated promptly by digitalis, diuretics, sedatives, oxygen and heparin. She recovered within a period of 4 weeks and was discharged from the hospital 6 weeks after admission.

Serial histological sections of the fallopian tubes (Figs. 2, 3, 4) showed features of chronic salpingitis and normal ovarian structure in the left ovary.

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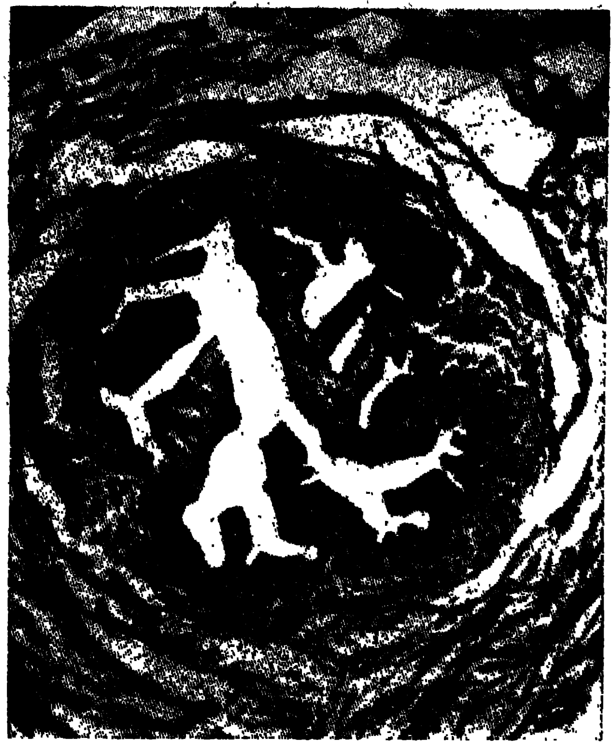


Fig. 2—Showing Photomicrograph with the Right Fallopian Tube without any Evidence of Recent or Remote Pregnancy

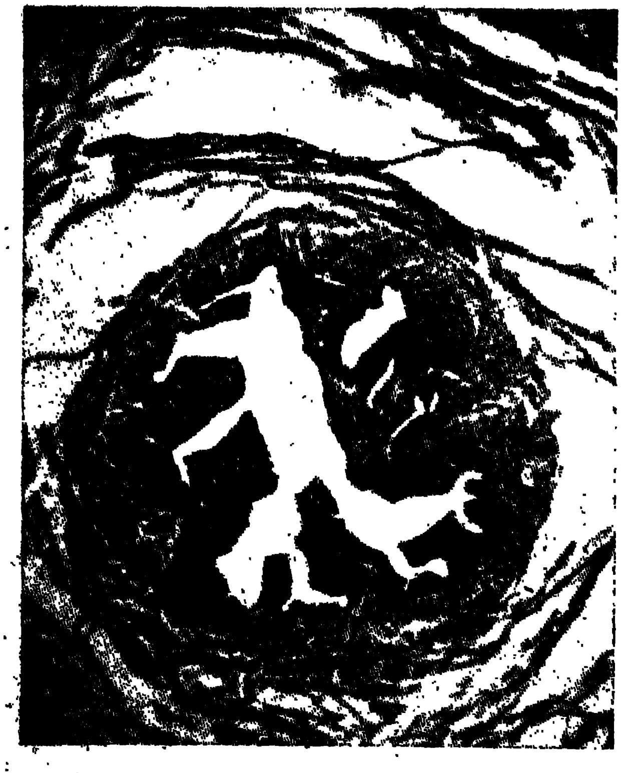


Fig. 3—Showing Photomicrograph of the Left Fallopian Tube Without any Evidence of Recent or Remote Pregnancy

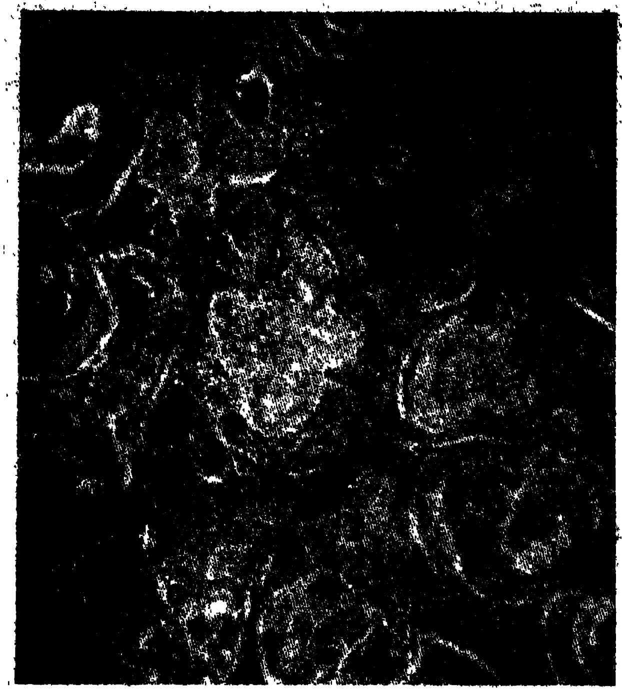


Fig. 4—Showing Photomicrograph of the Left Ovary with Normal Structure

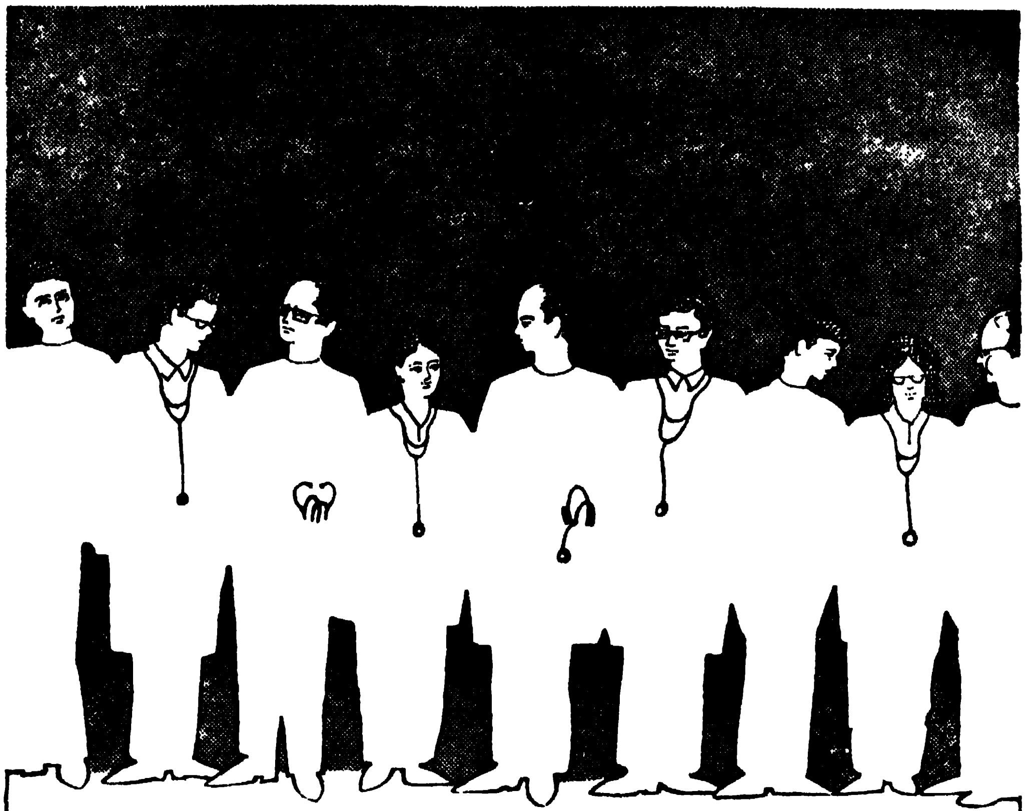
Discussion

From the history, laparotomy findings and histological reports of the tubes and left ovary the case was diagnosed as primary abdominal pregnancy, complicated by intestinal obstruction.

Beacham and his colleagues (1962) at Charity Hospital in New Orleans cite the incidence of abdominal pregnancy as 1 in 3,372 births and this is in close agreement with the figures supplied by Crawford and Ward (1957). But primary implantation of the ovum on the peritoneum is so rare that many authors have doubted its existence as indicated by Cavanagh (1958) in his extensive review until Studdiford (1961) presented a well documented case of primary abdominal pregnancy which suggests the following criteria to be fulfilled as a proof of such a pregnancy : 1. Normal tubes and ovaries with no evidence of any recent or remote injury. 2. Absence of any evidence of utero-peritoneal fistula. 3. Presence of a pregnancy related exclusively to the peritoneal surface and young enough to eliminate the possibility of secondary implantation following primary nidation in the tube.

Early rupture of a tubal pregnancy is the usual cause of abdominal pregnancy; Osiakina-Rojdestvenskaia (1938) studied the tubes from 100 cases of tubal gestation and found out different histopathological causes of tubes to account for tubal pregnancy. Hence, we removed both fallopian tubes, which looked normal without any evidence of rupture or tubal abortion, for histopathological examination which revealed only features of chronic salpingitis and nothing else.

King (1932) directed attention to a very rare cause



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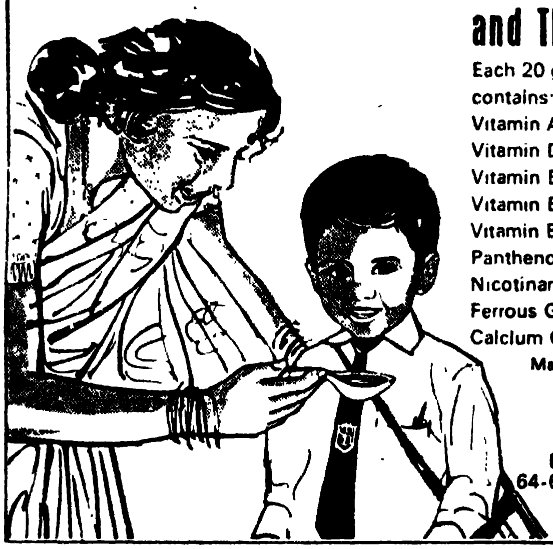

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ADVANCE

of abdominal pregnancy—postoperative separation of the uterine wound of a previous Caesarean section. But in this particular case 3 previous deliveries were normal and uneventful, so this possibility was excluded.

A majority of the foetuses die in the peritoneal cavity. Reviewing the world literature Ware (1948) cited a loss of about 75.6 per cent of foetuses. Beacham *et al.* (*loc. cit.*) cited a foetal loss of about 95 per cent in their series. The various bizarre termination of abdominal pregnancy including the type of case presented here have been discussed with illustrations by King (1954). Maternal mortality as cited by Ware (*loc. cit.*) was 14.5 per cent. Maternal mortality rate in a later period with improved operative technique and extensive use of transfusion was 6 per cent (Beacham *et al.*, *loc. cit.*) indicating that abdominal pregnancy is still one of the most formidable obstetric complications.

The final diagnosis was really made after laparotomy and histopathological examination of the tubes and ovaries. Cross *et al.* (1951) have emphasised that oxytocin test is the single most valuable test in the early diagnosis of abdominal pregnancy. The test is of value, particularly in advanced stages of pregnancy and only if contractions are clearly defined. But in the case presented here with intestinal obstruction and history of 14 weeks' pregnancy the said method of diagnosis was thought unnecessary. The case presented here has fulfilled the 3 important criteria of Studdiford (*loc. cit.*) as proof of primary abdominal pregnancy and hence the diagnosis.

ACKNOWLEDGMENT

The authors are grateful to Capt. P. K. Dutta, Superintendent, Chittaranjan Hospital, Calcutta National Medical College, for his kind permission to publish this case.

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2

Amoebic Abscess of the Spleen

D. SENGUPTA*, BINA MUKHERJEE**

Amoebiasis is an extremely common disease in the tropics. Amoebic affection of the spleen is, however, extremely rare. Amoebiasis is primarily intestinal. However, *Ent. histolytica*, being endowed with the property of secreting a proteolytic ferment (histolysin) and because it cannot thrive on dead tissues, constantly burrows through the comparatively healthy walls of the primary site, until and unless per chance it enters the radicle of a portal tributory. It thus reaches the liver, which forms the commonest metastatic site for *Ent. histolytica.* If the amoeba passes through the liver and lung filter, it enters the systemic circulation and can lodge in any organ. Pulmonary, pleuropulmonary, pericardial, cerebral and cutaneous amoebiasis, even lesions of the genital organs have been recorded in the literature. But by far the commonest extra-intestinal manifestation is hepatic amoebiasis.

But no definite record of splenic abscess alone, unassociated with hepatic abscess due to *Ent. histolytica,* has been found.

CASE REPORT

M. N. B., 28 years, Hindu, male, attended the outpatients' department of Calcutta Medical College Hospitals on 25-1-1972 with the complaints of heaviness in the abdomen—gradually increasing for the past 8 years, and weakness and low grade pyrexia for 1 week.

On examination, lymph nodes were not palpable. In the abdomen, there was a huge swelling in the left hypochondrium extending 6 inches below the costal margin. The mass measured 6 inches in the transverse diameter, had a smooth surface and was cystic in feel. The mass was not moveable in either of the axes and did not move with respiratory excursion. It was not tender. On percussion, it was dull and the dullness was continuous with splenic dullness.

Investigations—Hb, 11.5 g. per cent; R.B.C., 4.6 million/c.mm.; P.C.V., 35 per cent; W.B.C., 9000/c.mm.; polymorphs, 76 per cent; lymphocytes, 20 per cent; eosinophils, 2 per cent; and monocytes, 2 per cent. Toxic neutrophils were present (+). Blood urea, 30 mg./100 ml. Fasting blood sugar, 86 mg./100 ml. Urine, N.A.D.; stool, *Ent. histolytica* cysts present (+).

Barium meal x-ray examination revealed the stomach to be displaced to the right and anteriorly. Barium enema showed the splenic flexure displaced downwards. X-ray chest showed gross elevation of left dome of the diaphragm.

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I.V. pyelography showed marked displacement of left kidney downwards.

On splenic puncture, thick and chocolate coloured material was aspirated from the spleen, and the culture did not reveal any growth.

Casoni's test was negative.

Throughout the period of his stay in the hospital he had occasional attacks of low grade fever lasting for about a week; these attacks did not call for any specific treatment.

As the nature of the swelling was not quite clear an exploration was decided upon.

Surgery—A thoraco-abdominal incision was made through the bed of the left 8th rib. The spleen was found to be grossly enlarged with a huge cystic swelling with an opaque whitish wall. The surface was smooth and there were a few adhesions with the diaphragm, colon and stomach. The spleen was removed without much difficulty. The mass was sent to the Professor-Director of Pathology immediately under personal supervision for further study and diagnosis.

Pathology—The whole mass was about 11 inches in its longest vertical and about 9 inches in its longest horizontal diameters respectively. It consisted of a whitish opaque, smooth, noncongested, cystic, globular fluctuant swelling (about 7 inches × 8 inches), continuous laterally (i.e., towards the left) with a very thin rim of reddish layer of residual splenic tissue covered by the stretched fibrous (white) capsule of the spleen. The capsule was continuous all over the mass. In fact, the whole mass was contained within the splenic capsule but splenic material could be distinguished only at the upper and the lower poles and in the lateralmost part in the left side. A deep furrow indicated the splenic notch about 1½ inches proximal to its lower end. Splenic tissue, though small in amount, could be recognised at this region by its colour, consistency and capsule. The most protuberant portion of this mass was softer in consistency and was whiter than the rest. After surface sterilisation of this part, about 5 ml. of thick semiliquid material was aspirated in a sterile syringe and a portion from this material was inoculated in nutrient broth, nutrient agar and blood agar media for culture while the rest was divided into 2 portions and mixed with an equal proportion of fixatives, e.g., (1) formol saline and (2) Zenker's fluid respectively. The aspirated material was a combination of brownish red and white in colour. It reminded one of the classical description of 'anchovy-sauce' pus of an amoebic hepatic abscess.

The mass was bisected in a horizontal plane dividing it into 2 almost symmetrically corresponding halves (Fig. 1). The mass was one of a huge abscess cavity containing mostly a ragged, shaggy, disintegrated necrotic material, the centralmost portion being completely broken down. This portion did correspond to the soft protuberant area noticed in the specimen before it was bisected. The colour was greyish white, at some places whiter than the other portions; and was encircled by an area of thick whitish zone forming the wall of the cavity, separating it particularly at the upper and the lower poles from red zones of residual splenic tissue. This area, however, was not a fibrous capsule as can be seen from the photomicrograph of the histological section (Fig. 2) but consisted of necrotic splenic elements.

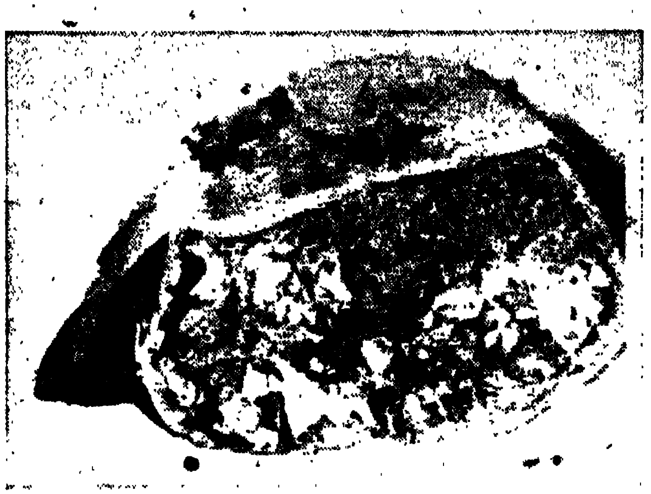

FIG. 1—SHOWING ABSCESS CAVITY IN THE SPLEEN WITH NECROTIC SLOUGH AND SOME SPLENIC TISSUE DISCERNIBLE AT BOTTOM

Scrapings from the wall of the cavity from several areas (8-10 sites) in particular from the area where splenic tissue could still be distinguished were collected for culture as well as for histological examination.

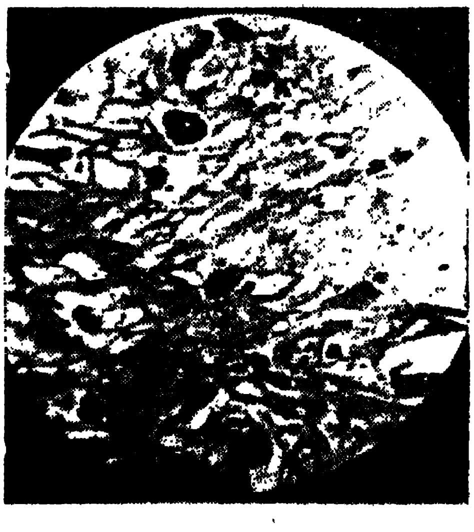

FIG. 2—SHOWING *Ent. histolytica* IN THE WALL OF THE ABSCESS CAVITY (*H & E 250*)

For histology, such scrapings were treated immediately with the fixatives, e.g., (1) 10 per cent formol saline and (2) Zenker's fluid. Wedge-shaped bits of tissues including splenic area and wall of the abscess were removed from 3-4 sites at the upper and lower poles and treated immediately with the above mentioned fixative solutions. The specimen was then immersed in a big bowl containing formol saline. After the tissue became fixed and hardened, another set of bits of tissue were taken on the following day.

Histology—From the 1st set of bits which were placed immediately in the fixative, the following observations could be made (Figs. 2, 3) :

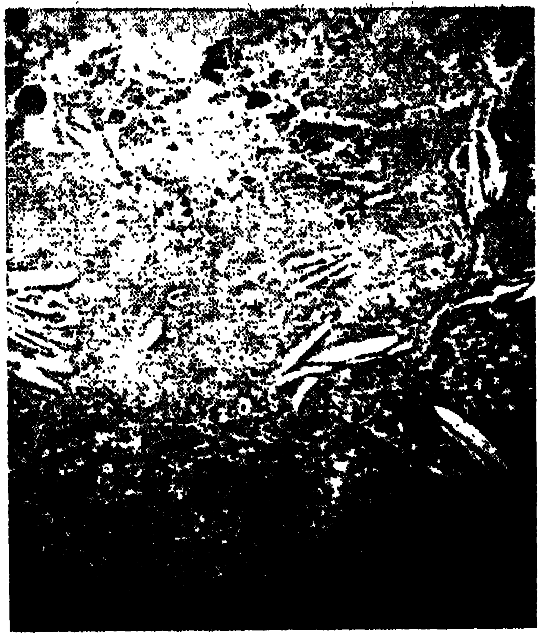

FIG. 3—SHOWING CHOLESTEROL CRYSTALS IN THE SPLEEN AND *Ent. histolytica* IN THE WALL OF THE ABSCESS CAVITY (*H & E×120*)

(a) The abscess cavity contained mainly necrotic material; no inflammatory cells were present.

(b) The wall of the abscess cavity showed numerous *Ent. histolytica.*

(c) The splenic tissue lost its normal architecture; only plenty of cholesterol crystals (also found in normal spleen) bore the evidence of its splenic nature.

(d) There was no evidence of fibrosis.

These observations were possible in the formalin-fixed as well as in the Zenker's fluid fixed samples and in haematoxylin-eosin stained preparations as well as in iron-haematoxylin stained preparations. But in the second set of tissue, bits which were processed after fixation and hardening of the whole specimen, i.e., after 48 hours of the removal the amoebae were extremely degenerated and could not be identified. The amoebae were recognised by the granularity of the eosinophilic cytoplasm, the distinct nuclear membrane and the central compact karyosome as it can be noticed also in Fig. 2.

Culture of the aspirated material was bacteriologically negative. Histological examination of the material showed only necrotic debris and no amoebae.

DISCUSSION

The present case had a huge abscess persisting for about 8 years without causing any symptom except the mechanical disadvantage due to the huge enlargement of the abdomen. A silent amoebic abscess of such a long duration has not been noted with hepatic abscess. In this case, perhaps it is the tough fibrous capsule that did not allow any breaking down of the abscess into the peritoneal cavity. It is interesting to note that even with a residual splenic tissue of about 1/8th the normal, the patient did not suffer from any specific symptom, suggesting once again that spleen is not an essential organ for life.

It may not be out of place to recollect that a number of meningo-encephalitis cases have recently been observed to be due to another amoeba species, and it is yet to be seen whether lesions in other organs could also be caused by these micro-organisms.

SUMMARY

A case of amoebic abscess of the spleen has been recorded. Fixation immediately after removal from the body is essential in order to demonstrate the amoebae. The possibility of 'amoeboma' of spleen should be borne in mind as one of the rare causes of huge enlargement of spleen.

ACKNOWLEDGMENT

We are grateful to Dr. S. N. De, Ex-Professor-Director, Department of Pathology and Bacteriology, Medical College, Calcutta, who kindly re-examined the slides and concurred with the diagnosis. Our thanks are also due to Dr. B. K. Chakraborty, Principal, Medical College, Calcutta, for his kind permission to publish this report. We are grateful to Dr. B. Chowdhuri, Curator of the Pathology and Bacteriology Museum, Medical College, Calcutta, for preserving the specimen.

3

Massive Intravenous Frusemide Therapy In Acute Renal Failure

MAM CHANDRA*, S. S. AGARWAL**
M. K. MITRA***, N. N. GUPTA****

The conservative treatment of acute renal failure continues to hold an important place in the management of this challenging problem, particularly where the facilities for dialysis are not available. Recently, massive intravenous frusemide therapy has been introduced (Silverberg *et al.*, 1970; Cantarovich *et al.*, 1971; Fries *et al.*, 1971; Sullivan *et al.*, 1971; Rizvi *et al.*, 1972) in the conservative treatment of acute renal failure. In this background we have conducted a trial to find out the role of massive intravenous frusemide therapy in acute renal failure. The summary of a representative case in which the highest dose of frusemide was used, is presented in this communication.

CASE REPORT

R.M., a 35-year-old female, multipara, resident of Lucknow, was admitted to the Queen Mary's Hospital, Lucknow, on 14-5-1973 as a case of infective hepatitis with incomplete abortion of 7 months' pregnancy. On admission she was having bleeding per vagina for 1 day and her blood pressure dropped to 80 mm. Hg (systolic). Evacuation was done by dilatation and curettage, and

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bleeding was controlled on the same day. She was kept on crystalline pencillin 2 million units, intramuscularly every 6 hours, 4 mg. dexamethasone solution in 1 ml. 8 hourly, intramuscularly, mephentine sulphate one ampoule intramuscularly 6 hourly and intravenous glucose saline. In spite of all these her 24 hour urine output was nil. On 15-5-1973, she was transferred to the medical unit for the treatment of acute renal failure.

On examination, she was fully conscious; temprature was 100°F; pulse rate was 110/minute, regular and of low volume; respiration was 24/minute, regular; and B.P. was 90/50 mm. Hg. She was anaemic, jaundiced with enlarged liver; 4 cm. below the costal margin in the mid clavicular line, it was smooth, firm and tender. A self retaining Foley's catheter was put in. Her 24 hour urine output was nil.

Investigations—Haemoglobin, 99 per cent; T.L.C., 9200/c.mm.; polymorphs, 78 per cent; lymphocytes, 22 per cent; P.C.V., 28 ml. per cent; ESR, 22 mm. in the 1st hour; serum proteins, 6.2 g. per cent; serum cholesterol, 264 mg. per cent; Van den Berg reaction, direct positive; serum bilirubin, 3.7 mg. per cent; thymol turbidity, 1 unit; alkaline phosphatase, 25.5 K.A. units; prothrombin concentration, 60 per cent, blood urea, 65 mg. per cent; serum creatinine, 11.8 mg. per cent; serum sodium, 140 mEq./l.; serum potassium, 4.8 mEq./l.; x-ray abdomen was normal.

Treatment—When in spite of proper hydration, urine output continued to be nil for 72 hours, massive intravenous frusemide therapy was started on 17.-5-1974. In addition to frusemide therapy, usual conservative management of acute renal failure, including strict intake-output maintenance, potassium free, protein restricted diet was started. Crystalline pencillin was continued for 7 days in the dosage mentioned above.

Frusemide therapy was started with an initial dose of 400 mg. frusemide in 200 ml. of 5 per cent glucose by intravenous route on the 1st day, with a subsequent increase in dosage by 400 mg. per day, till a 24 hour urine output of more than 1500 ml. was achieved. In the present case the desired diuretic response was obtained on the 5th day of therapy after administration of 2000 mg. frusemide on that day after which frusemide therapy was stopped. Urine output increased from 0 to 350 ml. on the first day of therapy, which subsequently rose upto 1950 ml. on the last day of therapy. In spite of a gradually increasing urine output, blood urea and serum creatinine continued to increase for the first few days. The diuretic response was sustained even after cessation of frusemide therapy. Blood urea increased from 65 mg. per cent to 188 mg. per cent and started coming down only on the 6th day of treatment, decreasing upto 30 mg. per cent on the 20th day of hospitalisation. Serum creatinine increased from 11.8 mg. per cent to 13.8 mg. per cent and started coming down on the 3rd day of frusemide therapy; decreasing upto 1.0 mg. per cent on the 28th day of hospitalisation. Creatinine clearance increased from 2.4 ml. per cent (on the 1st day of therapy) to 92.4 ml. per cent on the 28th day of hospitalisation. Liver function tests repeated 15 days after admission were normal. The patient was discharged cured on the 29th day of hospitalisation.

The patient expreinced transient deafness and tinnitus when 1200 mg. or more frusemide was administered. This toxic effect of frusemide was dependent on the size of the dose and duration of infusion. A careful supplement of fluid and electrolytes prevented the depletion of sodium and potassium during diuretic phase.

DISCUSSION

The aim of conservative treatment in acute renal failure is to maintain the internal environment within normal limits during oligo-anuric phase which usually persists for 7-21 days and occasionally may persist for as long as 60 days. Total duration of oligo-anuria has a definite correlation to the mortality rate in these patients (Stott *et al.*, 1972), which was higher with longer period of oligo-anuria.

Observations that frusemide therapy may induce diuresis even in patients with renal insufficiency (Berman and Ebrahim, 1963) have led to extensive trials in this field. It is evident in the present case that massive frusemide therapy has led to prompt diuresis and has cut short the period of oligo-anuria. Once the oligo-anuric phase is terminated and diuretic response is obtained, diuresis continues even after the stoppage of massive frusemide therapy, leading to a gradually progressive improvement in renal function.

After the onset of diuresis, there was definite clinical improvement in the general condition of the patient in spite of increasing blood urea levels for the first few days. This observation further supports the fact that symptoms of renal failure are not due to the high concentration of blood urea alone. In the present case, creatinine clearance test was found to be a satisfactory guide for the judgement of the state of renal function. Birtch *et al.* (1967) have put forward a hypothesis to explain the mechanism of action of frusemide in massive doses. They suggested that the redistribution of intrarenal blood flow was an important action of the drug which leads to increased blood flow to renal cortex resulting in an increase in glomerular filtration rate.

However, extensive trials are still required to confirm the mode of action and exact role of massive frusemide therapy in acute renal failure.

ACKNOWLEDGMENT

We gratefully acknowledge the help given by Mr. N. N. Tandon in various biochemical estimations.

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JOURNAL OF THE INDIAN MEDICAL ASSOCIATION

CALCUTTA, JANUARY 16, 1975

Rhinosporidiosis

Rhinosporidiosis is a fungal infection commonly of the mucosa of the nose, but extranasal sites may also be involved, such as, conjunctiva, ear, lacrimal sac, skin and genitalia, etc. Cases are being reported from different continents and subcontinents such as India, Ceylon, South America, Africa, Italy, etc. The first case of this disease was reported by Malbram in 1892 from Argentina in South America and its detailed report was published by Guillermo Seeber in 1900 after whom is the name of the aetiological agent, *Rhinosporidium seeberi*. In India, O'Kinealy (1894) was the first to report a case which was further studied by Minchin and Fantham[1] and they suggested the name of the fungal agent as *Rhinosporidium kinealyi*. Extranasal site of involvement has also been reported[2],[3],[4].

The disease is quite common in India and various authors have reported their series from different states. It has been observed that the disease is more common in southern, central and eastern states of India than northern states. Satyanaryana[5] reported a large series of 255 cases from Madras; Nanda *et al.*[6] reported 131 cases from Orissa; Purandare and Deoras[7] reported 100 cases from Bombay; Allen and Dave[4] reported 60 cases from M.P.; Sharma *et al.*[8] reported 57 cases from Nagpur; Das[9] reported 31 cases from West Bengal; Mohan Singh[10] reported 29 cases from Bihar. However, very few cases have been reported from northern India. This shows that most probably some regional factors play a part in the endemicity of the disease. Khan *et al.*[11] reported 41 cases from Bangladesh.

Rhinosporidium seeberi belongs to the lower group of fungi. Attempts to culture the fungus in the laboratory or reproduction of clinical infection in animals have failed so far. Rao[12] was successful in cultivating the fungi in sterile bovine dung at room temperature and subculturing it. There is still a vacuum left in the study of its mode of transmission, but the widely accepted hypothesis is by air or polluted water. Air or stagnant water is polluted from animal source (cow or horse dung). As the disease commonly involves nasal mucosa, the hypothesis of airborne infection is convincing. Swimming, diving and bathing in stagnant and polluted water is considered by some as the mode of transmission of the fungal spore[13]. *Rhinosporidium seeberi* has been demonstrated in the nostrils of domesticated animals, such as, horse, cattle, buffalo, etc.[14] Considering the high incidence of the disease among country dwellers, farmers and agriculturists—transmission through these domesticated animals is worth considering. Extranasal lesions are most probably transmitted through contaminated fingers or polluted water. Trauma is strongly suggested as a predisposing factor in the implantation of the transmitted fungal spore.

The infective spores, after implantation in the traumatised mucocutaneous area, enters deeper and leads a parasitic life[15]. In course of time the spores develop into sporangia by amitotic division or asexual multiplication. The sporangia may contain hundreds of spores and has a weak spot called "pore" wherefrom the spores are discharged into the tissues. The spores spread further into the tissues by way of lymphatics and pass into nasal secretion. The parasitic infestation leads to newly formed thin walled vascular spaces and cellular infiltration resulting in progressive increase of tissue element with development of polypoid tissue.

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Clinically, the disease is more common in males and occur in any age group, but predominantly between 11 and 40 years. The main presenting symptoms are nasal obstruction, nasal discharge, bleeding per nose, headache and itchiness of nose. The lesion presents as polypoid mass in the nasal cavity, arising from the lateral wall, anterior part of the septum, the middle and inferior turbinate, the floor or from multiple sites. The polypoid tissue appear vascular—pink or reddish in colour, friable, and bleeds on touch; the surface is studded with minute white dots. Sometimes, the polyp may protrude anteriorly through the nostrils or may extend posteriorly into the nasopharynx and hang in the oropharynx. Elsewhere in this issue[16], in an artirle on rhinoporidiosis, there are 2 cases mentioned where the polyp protruded through the nostril and in 1 case the mass was seen hanging in the oropharynx.

Histology is always confirmatory showing spores and sporangia in different stages in the epithelial and subepithelial zones, cellular infiltrate in the stroma and thin walled blood vessel formation.

Regarding treatment, complete excision with cauterisation of the base of the polyp is ideal. Chance of recurrence is minimal if the removal is complete. In cases where the growth has involved deeper part or has extended into the nasopharynx, chances of remnant may be there and recurrence is likely. As the disease can occur in multiple sites, growth *de novo* should also be considered in recurrence,

As the disease mainly involves the nasal mucosa and extranasal involvements are rare, the term "rhinosporidiosis" is still maintained. In this issue in the article "Rhinosporidiosis", the author[16] has suggested the general term "sporidiosis" which may be affixed or suffixed depending on the site of lesion such as "rhinosporidiosis" when nose is involved; "oculosporidiosis" when eye is involved; "otosporidiosis" when ear is involved, etc. This suggestion is worth considering, but in that case the name of the fungal agent should also be considered—whether to call it "*Sporidium seeberi*" and depending on the site of involvement, the name is to be affixed. So to avoid complexity of names, the old term, I think, should be maintained.

Shyamal K. De

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CURRENT MEDICAL LITERATURE

Alcohol: Its Use and Abuse

Norman, R. J. (*Cent. Afr. J. Med.*, **20**: 86, 1974) from Rhodesia writes;

The aim of this survey has been to highlight an exceedingly neglected medical and social problem in Rhodesia. It is right and proper to get worked up about other newer forms of drug addiction, but it should not be at the expense of a problem that has always been with us. Amidst emotional speeches on drugs, such as *dagga*, in Parliament in recent years it was refreshing to read that Senator Strong had taken note of the problem of alcoholism.

"It is the most sérious menace in Rhodesia today", he said, "Fifty times more people are hooked on the bottle as on drugs". Dr. Stamps, too, has written "Marijuana (*dagga*) has become the *bête-noir* of the responsible authorities, but it is questionable whether the real problem lies in this field—surely it is time to reappraise our attitude towards the promotion of this drug (alcohol) in the community".

Public concern about alcohol consumption is not commensurate with the extent of the problem in this country, despite the fact that a few voluntary organisations provide the most realistic and informed treatment facilities possible considering their small budgets. The local alcohol manufacturers continue to deny that there are any problems due to abuse of their products and refuse to support research and rehabilitation programmes (Rhodesian Breweries who made a $2½ million profit in 1970 gave $50,00 in that year; African Distilleries contributed nothing). It is time that, at least in medical circles, people expressed concern about the permissive attitude to alcohol abuse in our society and initiated a programme that would "radically amend our social modes so that they eventually reflect a more honest and consistent attitude of caution towards this, one of the most dangerous of all addictive drugs".

The Hookworm Problem in the Rhodesian Lowveld

Goldsmid, J. M., Morrison, J. F. and Saunders, C. R. (*Cent. Afr. J. Med.*, **20**: 97, 1974) from the University of Rhodesia and Triangle Hospital comment:

The hookworm problem in the lowveld region is a complex one, involving *Necator americanus, Ancylostoma duodenale* and *Ternidens deminutus.*

While loads recorded were generally low, this fact plus the high prevalance, create a threat, unless the position is watched carefully. With the expansion of irrigation systems, the widespread hookworm infestation may develop into a widespread hookworm disease.

Although we were unable to demonstrate any significant difference in working capacity of labourers harbouring low and high loads of hookworm, it may be that such effects were masked by the multiple nature of most of the parasitic infestations.

Given a single dose regimen of 10 mg./kg. or 20 mg./kg. of pyrantel pamoate proved extremely safe and effective in the treatment of *Ternidens deminutus* and *Ancylostoma duodenale* infestations. For infestions with *Necator americanus*, a 3-day course of treatment is recommended.

Bone-Marrow Transplantation for Haematalogic Neoplasia

Fefer, A., Einstein, A. B., Thomas, E. D., Buckner, G. D., Clift, R. A., Glucksberg, H., Neiman, P. E. and Storb, R. (*New Eng. J. Med.*, **290**: 1389, 1974) from the Department of Medicine, Division of Oncology, University of Washington School of Medicine, Seattle, and the United States Public Health Service Hospital, Seattle, state:

Sixteen patients (11 years to 67 years of age) with haematologic neoplasia refractory to conventional therapy were treated with cyclophosphamide (60 mg. per kg. per day on 2 occasions), a supralethal dose of total-body irradiation (1000 rads) and a bone-marrow transplant from a normal identical twin. Twelve patients also received immunotherapy consisting of subcutaneous injections of the patients' own leukaemia cells lethally irradiated with 10,000 rads and intravenous infusions of peripheral blood lymphocytes from the normal twin. Fourteen patients experienced complete remissions. Six patients (2 with acute lymphoblastic leukaemia, 3 with acute myelogenous leukaemia, and one with lymphosarcoma-leukaemia) remained in complete remission at 11 to 44 months without any maintenance chemotherapy, and 2 others with acute myelogenous leukaemia were in complete remission at 2 and 3 months. One patient died of viral hepatitis without leukaemia. Five patients relapsed at 3 to 7 months. This approach can thus induce frequent and enduring remissions in end-stage patients.

Postpartum Reactions

Asch, S. S. and Rubin, L. J. (*Amer. J. Psychiat.*, **131**: 870, 1974) from the Department of Psychiatry, Mount Sinai School of Medicine, City University of New York, New York, state:

The authors describe four postpartum syndromes that are not often recognised, including infanticide and child battering, the grandmother reaction, the adoptive mother reaction and the father reaction. These reactions derive from experiences involving the person's mental representations of pregnancy, parturition, and motherhood and are not confined to the biological mother. The phenomenon of successive generations of postpartum reactions in women is described and explained as being grandmother-oriented. Awareness of this sequence should aid in the anticipation of postpartum psychopathology.

We have described 4 types of postpartum reactions that are easily overlooked. In one group, the mother's psychological reaction is made manifest by child battering or infanticide. The connection of the 3 other groups with pregnancy and delivery is usually missed since they involve someone other than the parturient: the husband, grandmother, or adoptive parents.

Similar reactions occur in successive generations of mothers—not through genetic transmission but rather by relatively specific psychological stimuli in early life; this does not, however, exclude the possibility of constitutional predisposition as well. Our case material adds to the literature that implicates in postpartum reactions the early mothering experience of the new parent, the vicissitudes of her separation and individuation from her mother, her sibling experience, and the nature of the oedipal resolution. These observations support the conclusion that postpartum reactions are primarily psychogenic, since we have described reactions in subjects whose hormonal and physiological changes were not involved because they were not parturients.

Bacterial Invasion of the Urinary Tract by way of the Vaginal route in the Rat

Dierauf, L. A., Gowdey, A. C. and Mulholland, G. (*Surg. Gynec. Obstet.*, **138**: 62, 1974) from the Department of Surgery, School of Medicine, University of Pennsylvania, Philadelphia, write:

Due to the relatively frequent clinical relationship between vaginal and lower urinary tract symptoms and infection, an investigation was undertaken to clarify the route of bacterial invasion of the lower part of the urinary tract. ^{99}mTc-labelled colloidal sulfur particles, analogous to bacteria, were used. Urethral luminal ascension could not be demonstrated by placing the radioactive particles on the external urethral meatus of female white rats. However, by placing ^{99}mTc-colloidal particles in the vagina, radioactive invasion was detected not only of the lower part of the urinary tract but also of the genital tract. This spread of particles in the anatomic region of the urogenital tract appears to be lymphatic in nature. These studies demonstrate the close association between the lower part of the urinary and lower part of the genital tracts as far as the spread of infection is concerned. Such a close association between the 2 systems suggests an important aspect of treatment in the control of infection of the lower part of the urinary tract.

Sulfone Resistance in Hansen's Disease

Jacobson, R. R. (*J. Christian Med. Ass. India.*, **49**: 210, 1974) from USPHS Hospital, Carville, Louisiana, USA, writes:

First of all, irregular intake of sulfones is more likely to lead to resistance than regular intake, and in our group of patients resistance occurred slightly later in those who took their medication faithfully. To promote regular intake, we recommend that dapsone be taken daily, and to decrease the incidence of resistance, that it be continued uninterrupted for life.

Secondly, our data suggests but does not prove that an oral intake of less than 100 mg. of dapsone or its equivalent weekly leads to the relatively early appearance of sulfone-resistant bacilli.

Thirdly, there is a strong possibility that any patient whose disease remains active over 10 years will eventually become sulfone-resistant, and he should be followed closely so that therapy can be changed as soon as indicated.

Fourthly, erythema nodosum leprosum (ENL) is probably not an important aetiologic factor in the appearance of sulfone-resistance except in so far as it leads to irregular therapy.

Lastly, among those whose bacilli were sensitive to sulfones at the start of therapy, resistance appears unlikely to occur except at the lepromatous end of the spectrum. We have not, for example, yet had a pure borderline case develop resistance.

NOTES AND NEWS

Formation of Health Co-operatives and Cadre of Multipurpose Workers proposed

Inaugurating the annual convention of the Indian Hospital Associations, Sri A. K. M. Ishaque, Union Deputy Minister for Health and Family Planning, said that Government of India had a scheme called 'One Third Scheme', to provide self-employment for health workers, who did not like Government jobs. The scheme envisaged formulation of 'health co-operatives' for which doctors, nurses as also para-medical workers were eligible and for which finances would be provided on one-third basis by the Union Government, State Government and members of co-operatives.

Sri Ishaque said that Government proposed to create a cadre of medical workers to be known as 'medical and health assistants' who would not be like the 'Chinese bare-foot doctors' but somewhat akin to the 'feldsher' of the U.S.S.R. These persons, he added, would be able to look after the common ailments for which curative skills were needed and would also provide simple preventive services like immunisation, health education and advice on family planning. The curriculum and other details of the scheme were being worked out.

Existing para-medical workers and nurses would be able to join the cadre of medical and health assistants after necessary education and induction programme, he said, adding that some of them, who possessed the requisite qualifications, might be able to join medical colleges and become medical graduates.

Fewer Autopsies Causting Setback to Medical Education

Dr. V. T H. Gunaratne, Regional Director of the South-East Asia regional office, World Health Organisation, recently said at New Delhi that medical education in several countries of the region was suffering most seriously because of too few or hardly any autopsy at all.

Inaugurating the silver jubilee conference of the Indian Association of Pathologists and Microbiologists, Dr. Gunaratne urged the association to contribute significantly to the medical education in the countries of South-East Asia by making available specimens of morbid tissues to departments of pathology in medical institutions there.

He said there was a pressing need for clinicians and pathologists to achieve high percentage of autopsies on patients whose lives could not be saved.

Symposium on Peptic Ulcer

A symposium on Peptic Ulcer was recently organised under the auspices of Doctors' Club, B. R. Singh Hospital, Calcutta on the occasion of its 4th Annual Scientific Conference. Dr. A. B. Mukerjee, Professor of Medicine, Calcutta National Medical College, presided and Prof. S. N. Sen, Vice-Chancellor, University of Calcutta, was present as the Chief Guest. Over 150 delegates from different parts of India and different zonal railways participated. Altogether 26 papers were read and followed by lively discussions.

The view was expressed that the incidence of peptic ulcer was increasing alarmingly. Of the many causes worries and anxieties, adulterated food, malnutrition, excessive smoking, irregular food habits and self-medications were described as the major ones.

Different sessions were chaired by Drs. A. B. Mukerjee, G. C. Mukherjee, K. C. Basu Mullick, G. S. Karai and Col. A. K. Ray.

Earlier Dr. F. W. Correa, Chief Medical Officer, Eastern Railway, inaugurated the conference and Dr. S. C. Kundu, Medical Superintendent, welcomed the guests.

Risks from Exposure to Trace Amount of Anaesthetics

Traces of anaesthetic gases present in hospital operating rooms affect the health of doctors and nurses, according to a survey by the American Society of Anaesthesiologists.

The survey has revealed that women operating room personnel repeatedly exposed to trace amounts of anaesthetic gases have a "significantly increased risk of spontaneous abortion, congenital abnormalities in their children, cancer, liver and kidney diseases". In the case of men there was an increase in liver diseases.

The survey covered 49,585 operating room personnel exposed to the gases and another 23,911 doctors and nurses not exposed to the operating room environment.

Despite the high incidence of diseases in operating room personnel the study concluded that so far "no cause and effect relationship between anaesthetic agents and disease had been proven".

OBITUARY

Dr. (Miss) Zubaidaben A. Merchant

Dr. (Miss) Zubaidaben A. Merchant passed away on 22-10-74 at the age of 35 following a brief illness. Born in 1939 she received her education at Bhavnagar and qualified for her M.B.B.S. degree in 1960 from Bombay. She obtained the D.G.O. in 1963 and M.D. in Obstetrics and Gynaecology is 1965. She served as a lady medical officer at Mahuva Municipal Hospital for a year and was later appointed as Chief Medical Officer at Nandkuvarba Hospital, Dhoraji, in 1966. Two years later she started her private maternity home at Bhavnagar.

A sports enthusiast in her college days, Dr. (Miss) Merchant represented her college in hockey during 1955-56. She also took keen interest in social welfare activities. She was connected with several maternal care and child welfare units at Bhavnagar as an honorary gynaecologist.

Dr. (Miss) Merchant was an active member of Bhavnagar Branch of I.M.A. and founder Secretary and later President of the Association of Women in Medical Profession. A good and devoted organiser of public health programmes she organised diagnostic camps at Gogha, Sihor, Tana, Gadhada and Bhavnagar, besides arranging educative lectures and film shows on health and family planning campaign. She endeared herself to all by her kind disposition.

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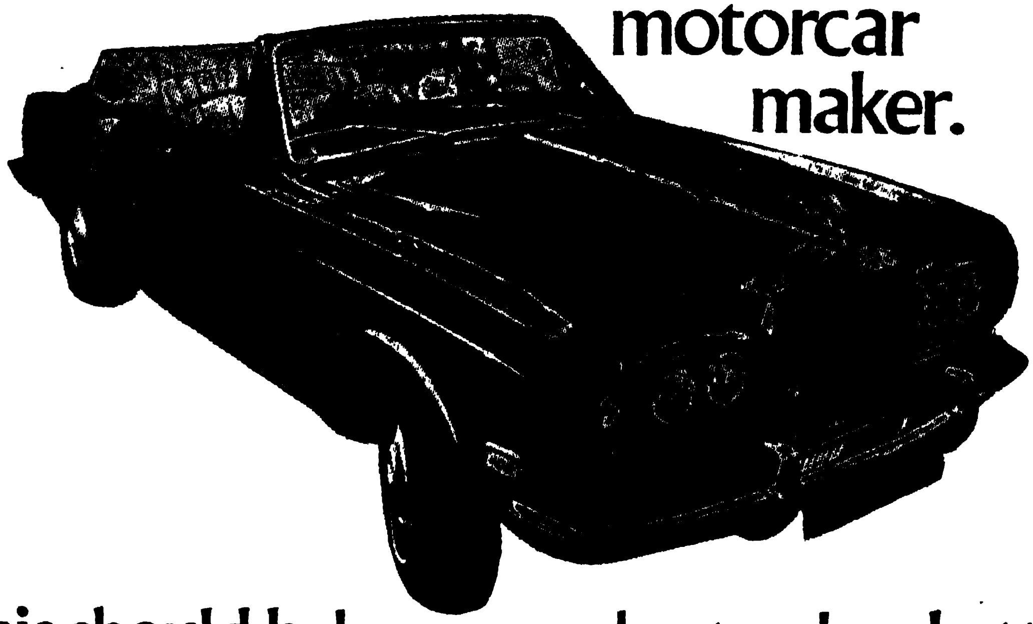

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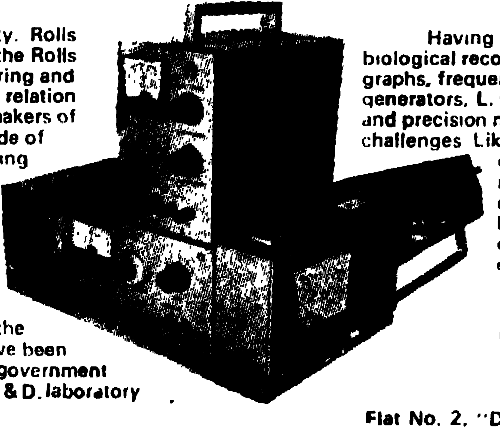

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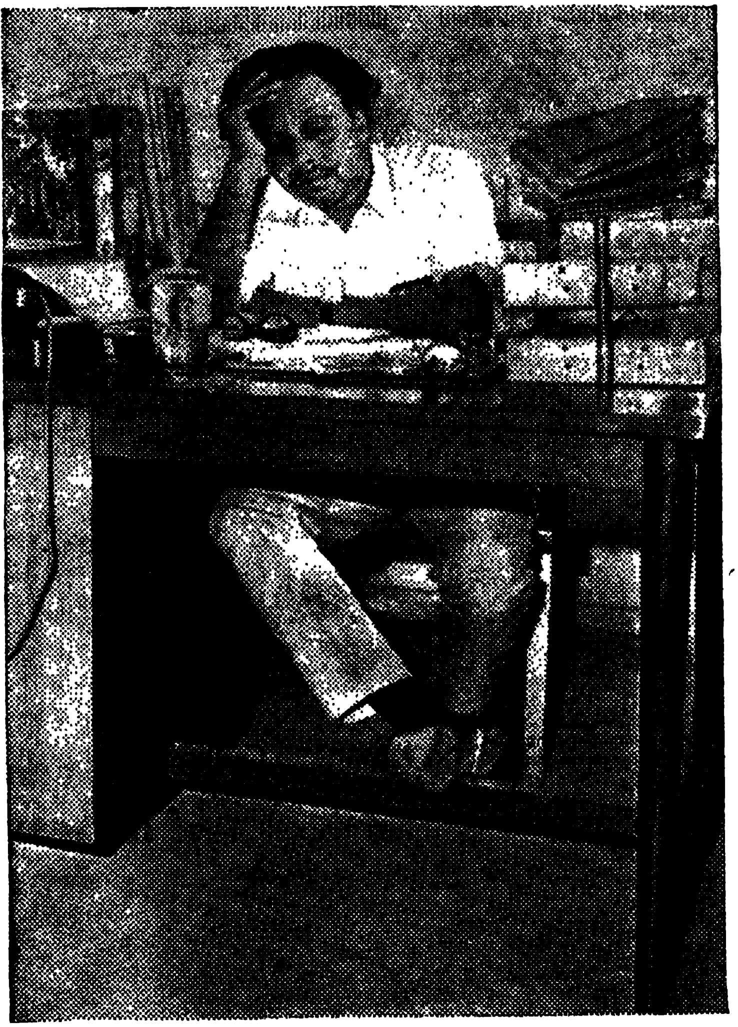

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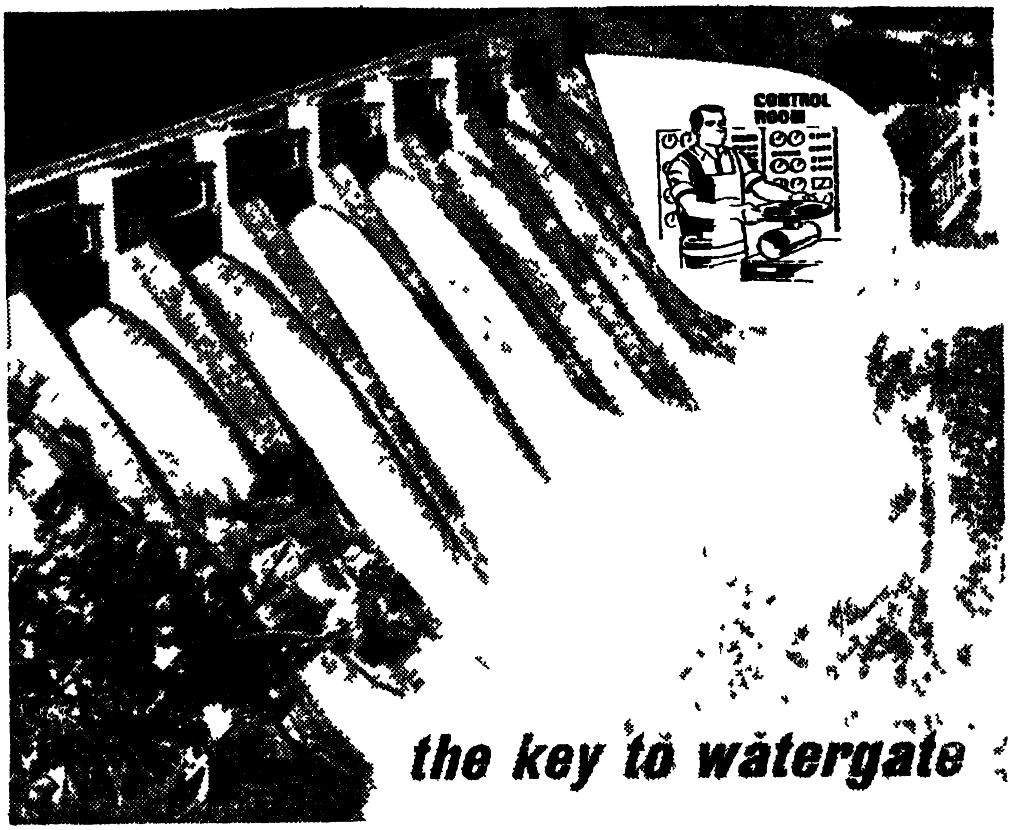

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Editor—Dr A B Mukerjee, M.D. (Cal.), F.R.C.P. (Lond.)